Breaking Strangleholds on Interdisciplinary Innovation

1 simple big idea in 3 points

all else is supporting evidence
ruthlessly culled from an
untapped ocean of it.

Why bother? ➔ see below and next the page

Main idea text ➔ overview starts after next page
Appendix Overview ➔ jump board to **Supporting Evidence**
Attachments Overview ➔ list of independently created documents

Video: Why is it Important?

First 5 min: trends in data science (has some jargon)
Last 5 min are on **Broader Science Challenges of our Time** (without jargon)
https://www.oreilly.com/ideas/jupyter-trends-in-2018
Slides at https://conferences.oreilly.com/jupyter/jup-ny/public/schedule/detail/71350
More talks at: https://conferences.oreilly.com/jupyter/jup-ny/public/schedule/proceedings

Not sure about timeliness or impact?

See cover and focus of ***Science*** from *Sept 21, 2018*
or the 'worldview' column in ***Nature*** from *Sept 27, 2018, p.435*

In case of questions

text me at 608-556-5594
I will find time to talk.
Have fun!

WID has been called 'a Great Wisconsin Experiment'

and as a part of it and as experimental biologist I have been wondering, who is keeping the LabJournal for this experiment we call 'WID'. Since I've never heard of anyone[1], I submit this as:

WID LabJournal, Entry X+1 Draft as of 2018-10 -09

by Laurence Loewe, first external Hire into WID Faculty.

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[1] That is after the Grand Opening Week in Dec 2010 where numerous relevant entries were presented as talks (and maybe more, I lost track). There was also some student who did some initial interviews with the early hires (may be 2011, latest 2012).

From: **Laurence 'Lion' Loewe**
To: **Jo Handelsman**, Wisconsin Institute for Discovery
CC: **Millard Susman, John Yin**
For: *Those fighting to break new ground through wide interdisciplinary diversity*
Date: WID, Madison, Sept 21, 2018, minor updates and expanded conclusions Oct 8, 2018
Subject: 'Dirt' or 'Soil' in WID, a *Great Wisconsin Experiment* serving the Wisconsin Idea

Why bother?

Highlights on this page are explained later.

This Summer, Millard and I deciphered how **the system of incentives that makes modern universities efficient in many ways stops key types of interdisciplinary research** by dis-incentivizing essential types of diversity. This doesn't have to be fate. We think a **tweak to university structure can stimulate the growth of such essential diversity** – without a need to abandon the responsible oversight and mentoring that have allowed modern universities to thrive.

I would like to invite your feedback on these ideas. For me, this is as urgent as you make it after reading it. As for myself, **I plan to publish the generally useful ideas from below** at some point in appropriately edited form. As excited as Millard and I are about our findings, **others will have to run with them.** **I serve science best if I focus on writing the best Evolvix I can.**

Please consider this text to be: (i) My late incomplete contribution to '*rescuing biomedical science,'* the 2014 workshop, where we first met [1]. **(ii)** An incomplete way to assist the 'giraffe'-style collaborations I suggested back then, see Appendix. **(iii)** **My incomplete surrogate 'tenure dossier'** – until I send to you my full dossier (*then* also to Genetics). I aimed to finish it asap at a consistent quality (before June for Genetics; after that for a broader audience & me). **Conceptual questions delayed me** (beyond my personal struggles). Poor dossiers are predictably rejected, *and* waste people's time; so *no dossier* is better! Thus, after failing to submit in time *despite my best efforts*, I took a closer look. My research program is more diverse than any I know; I felt **a broader root-cause analysis might help me to learn from mistakes** by understanding the bigger picture. Here I hoped to **give back to WID, as key discoveries I made relied on its broad interdisciplinary mission** (as I understood it). These analyses exceeded my 'minimal time to a poor dossier' (see my request from Feb 16, 2018). Their added value more than justified delays. I still aimed for a meaningful 'dossier with background', asap. **The new need to clear the pod puts this 'dossier evolution' on hold indefinitely.** I still hope to complete it – once I will have learned how to properly 'count' my full research output in 'official' metrics (without grotesquely exaggerating or cripplingly omitting). My interdisciplinary research is driven by **my goal** to provide my colleagues **in molecular and population genetics** the best computational system I can envision for **integrating all of genetics to mechanistically predict evolution**. I started to draw on ca. 16 disciplines (see Fig.0) to **leverage existing results** and accelerate implementation while improving it, albeit paying in time, space, and prestige. I found **integration is faster on paper in a big room packed with all info to facilitate many *random collisions of ideas* to smoothen** sharp edges of immature integrations; **such edges hurt in complex analyses and often cut beginners first, so smoothing is key!** It's the 'brain' of Evolvix architecture evolution and needs a stable space ca. the size of my pod. This pod usage did **take WID's principle of '*randomly colliding ideas*' to the next level**. Moving the system is delicate, parceling into storage near fatal. As requested, I've been developing an approach for moving it. **It's my firm goal to clear the pod by Oct 31** unless you quickly persuade me otherwise; once out, Evolvix will be implemented outside of WID. The move stops my search for best describing wide interdisciplinary work in a tenure dossier. **Others in WID need to continue this to get the interdisciplinary diversity required for user-friendly tools for hard problems like Fluxomix.**

To assist, I present a simple idea in 3 marked points, all else is supporting material.

It's not simplistic, but likely to work. It can help WID fundraising. **I hope you find this condensed summary useful. I can offer 1 revision of this text to your specs;** **else: I 'autoclave' the pod.**

No need to reply fast unless you want to. Appendix 0 has FYI questions I'll ask again in time.

Dear Jo,

Thank you for your patience and asking if I was happy with the dossier I wrote. Your question was a gem guiding me in a strange forest I did not see for all the trees that screamed for attention. It took time and Millard's help to see the forest, how it works, and its impact on WID's ability to conduct interdisciplinary research for complex problems, such as those faced in 'Fluxomix'. **Here I focus on a solution for root problems and what it might mean for WID**, omitting many pages on how Millard and I found it despite screaming trees. I am not in a position to change things. If labs are like petri-dishes, mine is about to be autoclaved.[2] I can only share what Millard and I got excited about. Perhaps there is a way WID can change 'forest growth'.

Opening the discussion

WID could be a key to a time that is pivotal for keeping our world together by celebrating its diversity. **WID** is in this position due to its ***wide interdisciplinary diversity*** **(*wid*)**, commitment to the ***Wisconsin Idea*** **(*WId*),** and the outstanding interdisciplinary research it already does at a university with huge diversity in disciplines and departments. Yet to fulfil the core of its interdisciplinary research mission, WID must pioneer ways for negotiating tensions between departmental needs for stability (undergraduate degrees can't change fast) and the necessarily uncomfortable alterity of *wid*, other disciplines, critical questions, and new perspectives.

In 2019 UW-Madison will update its 2009 self-study [2] to get accredited by HLCommission.org, likely reaffirming **two core values: (i) integrative interdisciplinary research, and (ii) the academic freedom for 'sifting and winnowing**...'. Such texts moved me to decline a position in Europe, join WID, embrace *wid*, and start a strategic interdisciplinary research program with an unusual *WId* core; I thought it was worth the risk because WID exists to break new ground and UW values diversity. Yet, universities today have reasons [3-7] to be structured in ways that **limit the academic freedom,** in particular for interdisciplinary research scientists and centers like WID; this relegates *wid* effectively to after-work hours, blocks promising *WId* projects, and explains institutional enigmas like 'why no computational biology degree?' or 'Madison did not start the UW data science MS in 2015'. The forces I identified are general and can easily torpedo 'Fluxomics' or other WID initiatives, even WID itself. This letter is about an idea to protect WID's ability to grow *wid*.

Problem

The root cause is **fundamental differences in the 'batching strategies'**[3] used for improving the efficiency of modern departments, which contrast with the batching required for efficient work on some interdisciplinary research questions. Such conflicts in strategy are independent of tenure, departmental details, discipline, university, or even country, as far as I can tell. The power of batching strategies is also seen in very different enterprises as observed by Conway's Law. [8-11] It states that "*organizations which design systems … are constrained to produce designs which are copies of the communication structures of these organizations*." [11] The impact is huge, as these constraints can easily keep optimal solutions from emerging – even when resources are not limiting. In my analysis, incentive structures can have

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[2] Coming to WID, choosing my interdisciplinary focus, *I knew the risks*. I am grateful for all opportunities I was given. I made discoveries I couldn't have dreamt of, shaping my future research. For me, my 'petri-dish lab' is like the strange **old petri-dish in Fleming's lab: to be autoclaved, yet it gave us antibiotics**. I can't do the follow-up work necessary for spelling out many valuable Evolvix insights I've seen, before evacuating the research pod I used at WID by Oct 31, the deadline I was given. Thus, **I will evacuate the pod by Oct 31** and continue Evolvix architecture work elsewhere.

[3] See notes in Appendix and Attachment Table of Content at the letter's end. If still unclear, I can explain in person.

similarly devastating effects on interdisciplinary research. The core problem is that **departments are incentivized to expect their faculty to adopt particular batching strategies** to improve their efficiency to an expected level; these can be very different from the batching strategies that may be required for solving particular interdisciplinary research problems of interest. I learned this the hard way. I combine three points into a solution and ask related questions (due to limited space for answers).

POINT 1: WID cannot accomplish its core interdisciplinary research mission efficiently in the long-term without the ability to grant tenure (see Appendices 1-2)

Without tenure rights, WID's potential for leveraging efficiencies in interdisciplinary research remains severely constrained because its researchers are not free to choose the best 'batching strategies' for the problems they study. All WID faculty to date are in principle and in practice under more or less tight control of their home departments, even after tenure. As a result,
WID's potential as an interdisciplinary research center is *conceptually* limited and in practice left to the mercy of disciplinary departments that are systemically incentivized to limit consciously or unconsciously how much interdisciplinarity they might want to tolerate among their tenured faculty in order to maintain the stability they need as departments. This tension may be exacerbated by separating the allocation of current or future resources required to pay for a new hire from assessing the risk entailed by a given research program. WID and departments tend to have very different views on the risks of a given research program and how to best handle them to serve their mission. Yet: **Who carries the risk?** Regardless of who pays for the risk, the other party is necessarily short-changed as long as the power to select research programs by hiring and making tenure decisions is separated from the responsibility to carry the risks. **Since departments are necessarily designed for more stability than research centers, a WID without tenure rights fights an uphill battle likely to limit the types of interdisciplinary research it can take on**, especially in the high-risk, high-reward class. As both WID and departments strive to produce world-class research, this is bound to remain a chronic source of tension that can at times even result in institutional warfare.

POINT 2: WID cannot grant tenure without a new department. Conventional ideas crown winning disciplines, hurt others. Only one idea is different. (see Appendices 2-4)

Tenure without departments would defy established expertise in how to organize universities (Appendix 2). Research centers like WID are meant to be dynamic and have no teaching mission; they necessarily have shorter expected life-spans than departments, which need stability to excel in teaching. Yet: **What department could WID possibly create?** The result of my analysis in Appendix 3 points surprisingly clearly to a single sensible outcome. It is easily summarized as:

WID needs a Department for Interdisciplinary Research (DIR) that focuses on the meta-research needed to improve the efficiency of interdisciplinary research itself.

Thus, the subject of study and teaching of a DIR is how to efficiently conduct interdisciplinary research itself. In my experience, there are many pressing questions waiting for a DIR to explore:

- Under which conditions can some types of interdisciplinary research and *wid* flourish?
- Which approaches, techniques, or skills are general enough for teaching how to facilitate interdisciplinary research, regardless of the particular disciplines and questions involved?

- Is it possible to produce starter kits for introducing *disciplinary* researchers faster to *wid*?
- Are particular challenges making some types of interdisciplinary research harder than others and how might frequent stumbling blocks be avoided, especially at the math-bio interface?
- Which safe-guards can protect *wid* participants from exceeding their frustration tolerance?
- How can new faculty best navigate the challenges of establishing *wid* learning courses?

Such questions could easily be investigated efficiently at WID if anybody were to try by meta-**analyzing ongoing interdisciplinary research that is already part of WID.** For now, an efficient DIR likely depends on a big center like WID that is happy to experiment. This ensures a big pool of experiences that are easy to tap into for starting work at a DIR and developing useful lines of inquiry that may be harder to establish without such a center.[4] WID has been called '*a Great Wisconsin Experiment*', **but who writes its lab notebook**? DIR scientists could **record what can be learned from the highs and lows of ongoing research at WID about how to make interdisciplinary research more efficient in general.** Such meta-analyses can start with informal records; over time a DIR will develop more formal tools to address increasingly nuanced questions and disciplinary combinations. Starting to **accumulate the lessons learned in ongoing interdisciplinary research is arguably one of the highest research priorities today:** most grand research challenges of today require *wid* and efficient interdisciplinary research, but:

we can't improve efficiency without properly reflecting on what works and what doesn't. Distilling lessons learned will naturally lead to related **service** (e.g., debugging collaborations at UW-Madison), **outreach** (e.g., conferences and short courses), and importantly: **teaching**. I could say much, but here is not the place to develop curricula. Overall, **students would learn how to (i)** efficiently *enter new disciplines*, **(ii)** robustly *reduce misunderstandings* that interfere as diverse disciplines and cultures try to communicate across *wid*, and **(iii)** *appreciate disciplines* with diverse strengths and limits. As DIRs recognize and nurture diverse types of *wid*, DIRs will likely **learn to leverage the abilities of today's polymaths** by defining how to recognize, educate, and engage them in grand research challenges that require *wid*. To engage polymaths, they too need clear career paths in academia and realistic chances for tenure. Currently, no such path exists. In today's universities, polymaths are either academically murdered or starved to death – a global problem as far as I can tell; their absence is unlikely due to genetic reasons.[5]

The mission of a DIR is to focus on meta-research investigating ongoing interdisciplinary research and how to improve it in WID, UW-Madison, and beyond via teaching, service, and outreach. A DIR led by the director of WID could enable both units to leverage many synergies and would only require minor tweaks to what has already been put in place through WID. The resulting institutional and meta-research innovation would provide a huge return on investment for WID and the campus. It could easily catapult WID into a global *wid* leadership position and make it easier to answer the big donor question about why to invest in WID (as opposed to better known Starvard-Oxbridge establishments).

In my analysis, questions only remain about how to *best* implement DIR, not about *whether* it's worth doing. **Returns on investment will likely to be huge for many reasonable implementations.** For example, a DIR could make valuable contributions to more reasonably justified credibility in academia and beyond, reducing unnecessary confusion (see Appendix 4).

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[4] Institutional inertia may cause other departments to overly hesitate, jeopardizing the start of a DIR that is at its best.

[5] As a geneticist, I doubt 'the last polymath' lived in the 19th century (e.g. Helmholtz; see *Nature* 2018, 561:175); I see no reason why the genes causing their abilities should be broken now. It seems more likely that modern universities can't handle them. Trying to sort Helmholtz's work into the career paths of modern departments proves the point.

POINT 3: Starting a DIR in WID is workable, timely, and improves efficiency. WID needs a DIR that studies *wid* and interdisciplinary research at WID in support of the *WId*.

The unusual idea of a DIR to support WID raises many questions: when, how, and with whom to implement? For brevity, I only list questions; many answers are likely obvious to you (I'll also happily share what I have). To narrow the scope, I tailored the questions specifically to WID;
I think that a WID-like center is needed or likely ideal to give a DIR a good start; **WID in its present state and at this exact time is an ideal springboard for a DIR.** I found many reasons for thinking that acting soon might produce the best outcomes and that results are achievable with a **reasonable effort at a low risk** in the current context of WID. **Many paths exist to a DIR** in WID, I found some more effective than others; **making it into the accreditation documents for 2019 would likely be ideal** if possible.
Here are practical questions to consider:

- **How much effort** is it to start a DIR at WID? Minimal effort? Would a pilot need less effort?
- **If DIR in WID starts big**[6] … Can it impress? How? What if it fails? Risks? Is bigger better?
- **If DIR in WID starts small**[7]… **How many faculty members does it take** (beyond a chair)? What is the smallest and fastest effort that can make a pilot work? Can a small DIR impress?
  What can go wrong? Who *would* know or *need to* know? What degree is easiest to pilot? Which advantages of big-starts do small-starts not share? do they matter?
  Which disadvantages of big-starts do small-starts not share? how important are they?
  What do students of a big-starts offer to employers that small-starts do not? how strategic?
  What is riskier for the DIR idea: start big or small? Which risks matter? for how long?
- **Initial faculty members:**[8] How to recruit? What would be the easiest way?

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[6] **If DIR in WID starts big**: **Can it impress? How?** Or else? **Risks?** Advantages? Effort needed? Disadvantages? **Perceptions?** (in local press? on campus? in UW departments losing faculty? in other UW departments? among peer institutions, or other WID-like centers, funders, donors, students, employers?) How would faculty divide up teaching before starting? Will PR be needed to get students? At which level to start teaching (B, M, PhD)? How to get accreditation in time to start with courses for many students? **Who respects their degrees? Would other interdisciplinary researchers in the US like a big-splash DIR at WID or likely antagonize it?**

[7] **If DIR in WID starts small:** Could a '**special committee degree'** work to delay the need for accreditation? Perceptions: can a near invisible pilot start and collect experiences, test ideas and if need be, die silent? **How silent can it be? Any unavoidable publicity? Would a small start evoke less antagonism among UW departments?** Which peer institutions or interdisciplinary researchers in the field would be annoyed/excited? **Which UW stakeholders already study *wid* interdisciplinary** research, maybe in part? **Who compiled the work presented in the 1-week of WID opening celebrations**? Which departments housed their work? Does a pilot cause the least waves by informing or inviting, before-or-after the pilot run? Whom might a small DIR embarrass? Could that be changed? Would a small DIR pilot failure be worse than failure of a big DIR? How much work is it to clean up a small DIR in the worst case?

[8] **Initial faculty members:** **How to recruit? What would be the easiest way?** Who joins not-yet departments? Who remains excited despite risk of closure? Who is willing to tolerate the excess risks of tenure guideline evolution, which is needed to avoid sloppy precedents? **What mentoring would be needed on the tenure track? and after? Who could mentor? who would? Which specific mentoring guidelines are needed? how develop them?** Would a senior figure come without overcommitting WID community or resources? How many in campus search committees see past a CV with many disciplines to spot someone who is good at observing and debugging interdisciplinary research, or helping others to do it? How many disciplines are DIR members expected to 'feel comfortable with'/'know', ...? Is it easier to hire externally for tenure-track? Or locally someone tenured? Or start with untenured lecturers? Which type fits best into WID? How many of the 20 WID lines might a DIR in WID be worth? Can DIR faculty lines be found outside WID? How long until advertisement for external hires? How long until external hires can start? What would necessarily have to be prepared? Same for internal hires? **How much faster could internal hires be?** Are there any suitable candidates? **Which criteria for tenure in DIR should be required? Which flexibilities should be allowed?**

- **Which core skills do DIR faculty need?** Any min-number of: disciplines exposed to? fields with publications? divisional committees they must pass to prove they can integrate?
  Same package for all, or new intro for each division? Allow non-integrative dossiers?
  How do challenges of developing innovative user-friendly service systems count? Or new software that crosses several disciplinary boundaries? Which literacies? How much Compute- Scientific- Math- Stats- Data- Humanities- SocialSci- Bio- Logic- Coding- etc. Literacy will be needed?
- **Department organization:** How much admin overhead to start a department?
  Can that be done in ‘pilot-mode’ to test it out together with a ‘pilot degree’, allowing both to fail silently if need be? What else can be done to minimize institutional risk (and clutter)?
- **Is it really possible to imagine a DIR chair who is not also the director of WID?**
  No; but how many h/month does this extra chair job need as DIR grows from start to
  (i) dept exists (ii) first hire (iii) first students (iv) first graduation (v) end of pilot?
  (vi) how does this scale with more faculty members? (vii) other scaling factors?
  (viii) can this be done in a realistic workload for a WID director?
- **How to overcome institutional inertia?** and get a DIR implemented in WID at UW? When is this best mentioned to potential donors? Before or after a pilot experiment?

That was it: *one* idea to tweak university structure, explained in *three* points.

All else below is supporting evidence, including the various appendices and attachments.

Pros & Cons

It would be easy to add a very long discussion of all pros and cons. Most of it would be quite obvious to you. As far as I can see, the pros win easily – if and only if such a DIR *can* be implemented with a reasonable effort to test the waters. A quick web search reveals on Google

"Department of Interdisciplinary Research"	ca 212,000 hits, and
"Department of Interdisciplinary Studies"	ca 450,000 hits,

some of the latter even seem to point to such a department in the UW-Madison School of Human Ecology, but it is no longer listed on the school’s website. From my cursory search I easily found organizational units with a ‘DIR related name’ that have disappeared again; on checking, these were ‘DIR by name only’: they did research that integrated several disciplines (as WID does too); however, they did not – as far as I can tell – leverage such work for meta-research studying what might improve the efficiency of interdisciplinary research. Most cutting-edge meta-research of this type seems scattered across all sorts of departments in various universities. This conceptual confusion that presents itself to distant observers may indicate much interest yet little general knowledge about which type of interdisciplinary research might advance which type of question most efficiently. The humanities and other disciplines studying human thought seem to embrace ‘interdisciplinary’ scholarship more easily than sciences. A more thorough analysis would be necessary for determining how many departments with ‘interdisciplinary’ in their name actually engage in meta-research on interdisciplinary research. It is not clear how thorough such an analysis would have to be to decide on starting a DIR in WID, as WID and UW-Madison would be winning either way. If any question existed about the timeliness and importance of such research, then the issue of Science from Sept 21, 2018 may provide some clarity [12-16]. Below I highlight questions of particular interest, which research in a DIR could address and that might improve the overall efficiency of UW-Madison.

Do more diverse faculty members also need more diverse measures of success?

Overall, in *searching for excellence & diversity* as UW-Madison aspires to become '*the model*' for a public research university, "*We need diversity in discipline, intellectual outlook, cognitive style, and personality to offer students the breadth of ideas that constitutes a dynamic intellectual community.*" [17] I could not agree more. I would like to state the need for the same thoroughness when it comes to recognizing **more diverse research products**, supporting **more diverse 'batching strategies'**, and developing more **versatile communication and supervision** methods. Without such diversity of approaches in these other areas, new and old WID faculty with the *wid* skills needed for key *WId* projects will continue to face a forced choice – if they consider research that engages in *wid* for WID goals, maybe it also serves the research in their department, but involves too much practical activity on the ground that requires a level of diversity judged as '*too much, no longer us*' by the power-brokers of a department. The alternatives are stark:

- more interdisciplinary research as best for WID (making tenure unlikely as conflicts with the department are pre-programmed; tenure does not change the stress levels much, if such faculty are continually harassed with annual performance reviews that are set up as 'penalties to be avoided'); or
- less interdisciplinary research to increase the likelihood of disciplinary tenure but effectively limiting the potential of WID for addressing important types of research problems that require certain types of *wid* – at least in my experience.

Curiously, the diversity and complexity of choosing paths in research and the implicitness and speed at which some self-censoring of research can occur, will often mean, that these choices are invisible to the outside world, and in many cases also even to those involved.

Thus, unless WID learns how to encourage such types of research, and learn from experiments such as my work in pushing the boundaries of interdisciplinary research, others might be likely to repeat these very costly mistakes. 'Glue-positions' could help with this, however, in my analysis they are likely too weak for the forces at play; they also cannot contribute to arguing for institutional stability in the same way as a DIR could. **Many reasons exist for why it takes a well-designed DIR-effort for breaking the new ground necessary to protect *wid* in WID's interdisciplinary research mission.**

DIR could propel WID to new levels of leadership in academia and beyond by reviving *WId*, but not without learning first how to handle *wid* communication challenges (Appendix 4). Without a DIR, I am deeply worried that the present and clear dangers for interdisciplinary research scientists embracing *wid* in academia will keep us globally from drawing vital links across domains in interdisciplinary research as necessary for solving the key problems of our time. The importance of input from a unit like a DIR is difficult to overstate if metrics shall be defined, used, and interpreted in ways that are *reasonably adequate* for a given research program and *support the emergence* of productive 'hot streaks' [18] instead of only rewarding them afterwards. It is well known that metrics currently struggle to do so.

Metric inaccuracy and the consequences for research

The metrics problem a DIR could help to solve is, in a nutshell, to decide, when two research metrics are to each other like 'apples and oranges' (i.e. not comparable), and when both can be summarized as 'fruits' (i.e. they are comparable without loss of adequacy for the underpinning research problems). Defining metrics well requires a lot of skill, and it is not clear that the widely used existing metrics in academia deserve the prominence they often continue to receive despite severe and well-known criticisms. Developing better metrics is a difficult meta-research problem with close connections to type theory and mathematical foundations, as well as the anthropological observation of what researchers actually do.

Academic freedom

There is a substantial literature documenting the increasing limitations of academic freedom [4-7]. They may not be deliberate willful prohibitions, but they are no less powerful prohibitors of important research and frustraters of next-generation scientists [19-23]. Who is encouraging scientists to "try new paths" [24]? Web of Science has a single article with these words in the title [24] (unless I overlooked something). Useful books and tips exist [25-27], but that does not mean they are widely known or that their recommendations are often supported by universities. In a context, where everybody has to look 'smart', research can become very complicated [28]; see also quote by Galbraith in Appendix 4. How organizations are set up, and therefore which batching strategies they can support is surprisingly important, as discussed elsewhere [29] and shown by Conway's law (see above). Metrics are an important part of the frustration that restricts the types of research that are possible. [30]. All these gradual changes have been combining into a perfect storm that changed a very powerful research culture into something the scientific heroes of old would struggle to recognize again [31].

"WHATEVER MAY BE THE LIMITATIONS WHICH TRAMMEL INQUIRY ELSEWHERE, WE BELIEVE THAT THE GREAT STATE UNIVERSITY OF WISCONSIN SHOULD EVER ENCOURAGE THAT CONTINUAL AND FEARLESS SIFTING AND WINNOWING BY WHICH ALONE THE TRUTH CAN BE FOUND." (TAKEN FROM A REPORT OF THE BOARD OF REGENTS IN 1894)
MEMORIAL, CLASS OF 1910.

What does '*Encouraging Academic Freedom*' mean *today*? A recent survey shows that PIs with tenure in my age-bracket typically conduct research in ~30% of their work time; they need the other 70% for submitting grants, revising papers, teaching, administrative work, and since recently also 'data storage' (5%) [22]. If overtime is defined as working more than 40h/week for *some* full-time jobs, and faculty members at UW-Madison work 60-70h/week on average, then these statistics might raise the question: **Why is academic freedom in research for professors in the US effectively limited to the equivalents of what would be called 'after-work hours' or 'overtime' in other jobs?** Clearly, it's not that simple, but the 'metric' is striking. This may also not be the end of it, as many scientists reported that the amount of administrative duties had significantly increased in the last 5 years [22]. **Overreliance on metrics** overestimates the ability of machines to implement justice. The use of metrics moves the power from responsible agents who can think ('people') to irresponsible agents who can only do *exactly* as told ('machines'). Humans are imperfect and can be unfair; however, the development of fair metrics requires solving the problem of developing an extraordinarily complex type system including fair conversions between types – a problem that computer science would shy away from. The disastrous social consequences are slowly emerging [32-34]. That doesn't mean, all metrics are bad. It just means that 'counting' is difficult and that the authors of *Principia mathematica* [35] had good reasons to place ca. 360 pages of complicated foundational math before they could claim: therefore: 1+1 = 2. To quote Einstein:
Not everything that matters can be measured and not everything that can be measured matters.

If these analyses are correct, then I am likely not the only researcher in WID who struggled to get tenure. Indeed, that seems to be the case. Other reports confirm these trends [31][20].

Madison has local heroes, such as Nobel laureates, or those who broke new ground, such as Jamie Thompson. I asked Dr. Thompson, if he could have done what he did on the tenure track. His answer was instructive and short: 'It would not have worked'. It was also surprising to find an analysis of a local UW researcher [4] who concluded in 1998 that Howard Temin likely would not have received tenure in 1998 if he had gone against majority opinion in 1998 as he did in his time a generation earlier. His opposition would have made a modern department very uneasy [4]. Yet, it was this very different way of thinking and his insights that motivated his fight against the received wisdom of his time that won him a Nobel prize [4]!

Costs of doing nothing – a great opportunity lost!

In my assessment someone is bound to do this or at least attempt this. Depending on how it is done, the core idea might be boosted or burned for some time. In the former case WID might lose an opportunity to lead in an area of its core competencies, in the latter case WID might have to fight an up-hill battle for the opportunity to try (as many might point to negative experiences elsewhere). If not implemented at all, the world would be robbed of many positive innovations, yet almost nobody would notice. **WID's setup and interdisciplinary mission place it in a rare position for implementing DIR well**. Other aspects:

- **Interdisciplinarity is too important for the mission of WID to not explore this**. It is so deeply embedded into WID's vision and nature that unnecessarily narrowing WID's purpose might diminish its stature on campus – at least for those who happen to be at the 'excluded' end of the spectrum. When I joined WID as its first external hire, I was surprised by the huge expectations brought to the Discovery Building by diverse people. How to possibly meet such enormous and amorphous expectations to benefit the rest of campus has been puzzling me as direct collaborations on details can only go so far. The idea of 'data science' at its most general face value has much potential for the rest of the campus. Yet, data science is usually interpreted much more narrowly and is not by definition free from the challenges of interdisciplinary work. Without DIR expertise in structuring and nurturing collaborations between disciplines, many hopeful initiatives will likely be unprepared for frustrating disciplinary culture mismatches, which stymy interdisciplinary work fast when efficiency is expected.
- **The logic of DIR as 'glue' for departments in universities is compelling and will sooner or later be implemented by somebody**. If not, academia is risking to further marginalize itself by missed connections, lack of reproducibility, rediscovery and reinvention. The resulting limits for active expertise restrict the problems our world can solve – and frustrate *wid* researchers [36].
- **Without a DIR, the same challenges in collaboration continue to be addressed inefficiently.** For example, the Oct 2, 2018 report on how to advance data science (http://go.wisc.edu/csreport) could be read as an indication for the urgent need for more collaboration across various existing UW strengths and how to meet that need. While the proposal is certainly a potential step in the right direction, it addresses core problems only indirectly, inefficiently, and without resolving important intrinsic contradictions[9] despite its price tag. As if it wanted to illustrate the need for a DIR and better data science at the same time, it omits existing UW efforts clearly worth a mention on a 45-page report[10].
- **Generally, we continue to pay dearly** for an ongoing lack of a working interdisciplinary research communication protocol for professionally indicating various types and nuances of "Yes" and "No" in clear ways without compromising a respectful dialogue; this includes an inability to recover from

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[9] For example, it calls for a large restructuring to recruit a leader who should "*wake up thinking about computing and go to bed thinking about computing*" yet with little indication of the limits imposed on such thoughts by dean-like responsibilities.

[10] Over 80% of work in data science is 'data finding and cleaning' according to the NIH and many practitioners. This report omits the 'University of Wisconsin Data Science Degree' (https://datasciencedegree.wisconsin.edu/) and any mention of work in WID except acknowledging that '*Brian Yandell, co-director of the Data Science Hub at U-Madison*[sic]*, aided greatly as well.*' That might not be indicative, since '*A key contributor to this institute will be the Data Science Hub, part of the Wisconsin institute for Discovery*' as reported on its release on Oct 2 at https://news.wisc.edu/report-uw-madison-should-expand-computing-efforts/

complicated interdisciplinary research communication situations if human imperfections get in the way. We might learn from aviation control. It had to solve similar problems to stop plane crashes.

- **Loss of 'hot streaks' is expensive.** Research is most productive in 'hot streaks' that can occur at any time in a career [18]. Without a DIR learning to *support the emergence* of 'hot streaks' the initial stages of discovery required for nurturing hot streaks tend to be discriminated against.
- **The quant-bio divide remains.** Interdisciplinary research that requires expertise in a non-quantitative field (e.g. in biology, medicine, or journalism) and a quantitative area (e.g. in math, stats, or computing) is particularly fraught with problems from disciplinary disconnect. Calls over 10 decades for improving statistical education [37-47] and my own experiences [48] indicate that new approaches are worth trying.
- **Unbalanced meta-analyses and a further degradation of trust.** Recent analyses showed a rise of meta-analyses paid for by special interest groups with disastrous results for those interested in an unbiased overview of a field [49] exacerbated by problems with the reproducibility of biological data analyses [50]. These trends sow mistrust by devaluing scientific expertise [51] and are nearly impossible to counter without DIR expertise.

Much more could be said. While it is tempting to trash **experiments that 'did not work' as expected, I have found that these can provide much more powerful insights if leveraged by properly analyzing** them in context. It is of course much easier to push unexpected results away to avoid potentially uncomfortable conclusions – as I know from experiences I had before I joined WID.

Conclusions – My Next Steps

I am very grateful for the opportunity to develop my research program at WID and to share in its inter-disciplinary mission. **I could have never found my most exciting result in a department** focused on one or two disciplines **as I would have never allowed my work to become so broad and deep.** I needed WID's interdisciplinarity to allow myself to draw from the 16 disciplines (see Fig.0) I need to develop an architecture for Evolvix foundations. **Biology needs an efficient, durable, and future-oriented cyber-infrastructure** for the large-scale integration of data, models, and code. This became clear as I developed diverse complex models in evolutionary systems biology, including some aiming to accurately simulate tumor progression and how antibiotics usage policies may slow down resistance evolution. Yet, desiring high-impact results and committing to the research required to obtain them are two very different things – especially when leaving familiar departmental shorelines is essential for exploring a truly unknown open ocean. Challenges multiply for researchers when departments worry about disciplinary boundaries (as I learned the hard way). **If no DIR-like support exists for those who venture deep into the unknown, then some key answers for pressing problems will stay out of humanity's reach – unnecessarily. This problem is general.** Its analogous forms in industry have sunk great companies [52] by keeping their innovations from reaching the maturity expected by end-consumers. A recent study [52] showed that **to innovate on the long-term**, companies have to **focus on the mid-term.** In this awkward phase, **work on maturing products seems unproductive to most**, especially '**long-termers'** (who efficiently write research papers with little regard to practical usability) and '**short-termers'** (who efficiently sell tried and tested last-generation products to satisfy customers). **Few accept the uncertainty it takes to innovate.** The study found few companies who knew how **to protect the special leadership skills and resources needed for shepherding innovations** through their dangerous 'teenage' years [52]. The same issues are likely pivotal for many innovative *WId* projects that benefit from *wid* to innovate where it matters most.

I can certainly attest to these dynamics from my work on moving Evolvix from an academic prototype towards a stable tool for broad use across biology and beyond. I define the mission of Evolvix as to:

simplify accurate modeling of systems described in a stable extensible user-friendly language.

I found that success requires drawing efficiently on the results from many disciplines (see Fig.0), enough experience in computational biology for efficient '*prefactoring*' [53], the mental agility to engage beginners in biology as users (Fig.5), and an unusual degree of focus [54]. A well-known computer scientist warned that he found such focus difficult to reconcile with the demands of academic life [54], motivating him to retire early to complete the most important research of his life [55]. **The most exciting result I found in WID is how well the methodology works that I need for meeting the challenges of the Evolvix mission (Fig.5).** I know that I can focus myself sufficiently to get there; yet, despite my best efforts, I cannot reconcile efficient work on Evolvix with the batching strategies my department expects me to use before or after tenure. Thus, as much as I like academic life in Genetics and in WID (it's still my dream job), I have been becoming increasingly aware of a **stark choice**: Either (i) **I build on the most exciting research results I found in WID in the interest of genetics** (but would have to leave WID since I cannot also please my home department), **or** (ii) **I try to stay in WID** by pleasing my home department, which requires effectively abandoning my work on Evolvix. My evidence shows: **this dilemma is surprisingly independent** of my tenure status, home department, and other challenges I have been facing. *Thus, surprisingly, my home department may have just done me the favor of encouraging me to choose the better alternative in a very complex decision process*. Ideally, a DIR in WID would have been ready to help researchers like me to navigate these questions from the start (where it matters most). In my case, at least I know now what I would have lost if I had abandoned WID's interdisciplinary mission as I understood it. I am not sure I would have known if it was not for WID. **What next?** After moving out of the pod, as I said, I will finish the FlyClockbase series of 16 papers as fast as I can. It will be a detailed battle-cry for why we need a compiler for biodata science. Then **I will write that compiler**. After all, even in science I have to believe in something. Even if it means sacrificing everything.
I hope a DIR in WID can be established for those who need it more than I did.

All the best – and in particular for running WID,
Laurence

Afterthought –

On a still broader problem. *A report where a long-time senior editor of The Guardian asked* 'who broke the news*'* [56] *is commenting on metrics-based incentive systems in the news room. In his experience, investigative journalism is too slow, hard, and expensive to ever be justifiable by any metrics he saw for evaluating news-rooms. Yet, without such ground-breaking investigative journalism, newspapers become too predictable and slowly lose what people expect them to stand for in the long term. Thus, maybe*

news was broken by a dearth of ground-breaking investigations

whatever may have caused it. I would not be surprised if eventually a thorough meta-analysis of scientific research will draw analogous conclusions: opportunities for breaking new ground need protection, whether in journalism [56, 57]*, in industry* [52]*, or in academia* [55][and as I argue here]*. The overall importance of getting this right cannot be overestimated as aptly explained in the video on the front page.*

Ground breaking discoveries are made at **rock-bottom** more often than not. *They are risky, hard, and progress can be slow. They cannot be made while also aiming to collect as much low-hanging* *fruit as possible. I have collected and enjoyed a fair share of low-hanging fruit in my career. However, I also need the freedom to also engage with harder problems - as long as I can still see a way to attack them. The subtle, yet powerful incentives that aim to reduce risk in research can make such work prohibitive – at least they seem to do that in my case. A senior population genetics leader from Harvard once suggested a rule for funders that would expect more experienced faculty to no longer be allowed to submit lower-risk grants, which are for younger colleagues who need to establish themselves. Instead senior faculty should leverage their experience to attack the hardest problems. If he had interdisciplinary research in mind I do not know, but the same suggestion would likely also be useful for improving the quality of interdisciplinary research – if those engaging in these inherently riskier projects were not forced into comparisons with colleagues who can streamline their research more along disciplinary conventions.*

Grace Hopper, *who made it onto my attached list of 'Evolvix Giants of Biodata Science' for writing the world's first compiler, reportedly kept encouraging younger researchers repeatedly to take on riskier projects. This was maybe not surprising, given the huge career risks she accepted to get a chance for her pioneering work in creating the first programming language compiler that connected well to ordinary English (which was considered impossible by some experts at the time). Yet, Grace broke new ground that appeared unbreakable to others. Too many of these groundbreaking discoveries are probably taken too much for granted.*

Appendices Overview

Attachments

Attachments provided —— Table of Content —— Overviews of Dossier, Output Diversity, and Posters

A. **Fig.0 – Fig.5 embedded in an incomplete draft of my Tenure Dossier Overview Statements.**
These figures are cited in the frontmatter text; I finalized them for my tenure; in contrast, all other texts made it to an 'advanced draft stage'; I haven't yet cited references properly throughout. To finalize the narrative around the figures likely needs a round of external feedback or two. Given the need to clear the pod, neither is likely to happen. Without further feedback, **please consider the following to be 'my tenure dossier' submission you have been waiting for:**

1. **The frontmatter** with some appendices (not included, you have a printout).
2. **Attachments provided** - Table of Content (this overview page)
3. **Background** statement (and **Fig.0**: overview of the disciplines I draw from)
4. **Integration** statement (and **Fig.1**: ecological forecasts; see **Poster C1**for larger print)
5. **Research** statement (and **Fig.2**: game theory in Evolvix; **Fig.3**: biouncertainty measured)
6. **Teaching** statement (and **Fig.4**: influenza model from students in my course)
7. **Outreach** statement (and **Fig.5**: design flip method for developing new languages)
8. Service statement omitted (still to be completed)
9. **Proxy evidence** (most recent CV instead of incomplete lists of papers, grants, and more)
10. Introducing **my 4 2 representative publications** and 10 biased ways of selecting them

Numbering in the titles below follows the UW-Madison bio division guidelines.

B. **Output Diversity example explaining the challenges: Evolvix Giants of Biodata Science**
Illustrates the important recurrent case in my work where it evolves continually to improve by integrating important interdisciplinary insights and the challenges of how to 'count' it in the context of preparing tenure documents.

1. **Motivation for Evolvix Giants**: Why & how to use their list to reduce cognitive overload by memorably grouping related abstract concepts and assisting users with navigation.
2. **Quality Annotations of Evolvix Giants:** how to use key stages of Stabilizing Versioning in Evolvix: why they exist, and how they are used for content for various sections.
3. **My main responsibility as Architect of Evolvix.**
4. **Impact of *Batching Strategies* on progress with implementing Evolvix.**
5. **The actual content of the file 'Evolvix Giants of Biodata Science'**

C. **Other Output Diversity examples: some recent WID Symposium Posters and more**

1. **Poster: Ecological Forecasts** of Fox and Rabbit with Evolvix (larger than Fig.1 above)
2. **Poster: Interdisciplinarity** of my work as explained
3. **Poster: Why Biology needs its own language** for general-purpose programming
4. **Evolvix**: How to efficiently record time series.
5. **FlyClockbase**: Are VBIRs like FlyClockbase the new genome projects?
6. **Poster: My lab in WID** as described for the WID symposium
7. **Giraffe: different roles** in the scientific enterprise
8. **Interdisciplinary Discussion Starter** (I developed this for my course)

D. **Recent CV**

Attachments not provided

1. **My full tenure dossier**
   While some parts are as good as final (e.g., all Fig.0 – Fig.5, Integration Statement, and more), the overall state is too mixed quality to be presentable.
   Overall the format is too small for what I have to write if I indeed present all of my research and refrain from arbitrarily pretending I did only work in some area, but not others. Thus, much of it is like

   An attempt to fit a shepherd's dog into a shoebox.

   Nevertheless, I'm surprised how far I got, and it was definitively a useful exercise; I can see, why someone who wants to be a professor has to be able to do this.

   Yet, to appropriately present my work and feel happy about the state of the dossier, more fundamental questions need to be addressed that are beyond my remit to do. For example, I need to know how to deal with the systemic findings I've been reporting in this letter. Then there are outreach related pieces of work like the Giant's list provided as an example below that tick too many boxes to belong to any recognizable category I've seen in the guidelines. Then, I'm not sure how to report negative findings, of which I have many that were rather costly to get. Many fragments document my progress in writing Evolvix, but few fit the 'published-or-not' dualism that prevails in most departments.
   Given the need to move my base of operations out of the pod, I will stop thinking about these questions for quite some time. Thus, I cannot promise to finish the dossier any time soon, but may try another go after finishing FlyClockbase as time permits. Once I have something more consistent for Genetics, you'd get it as well.
   Time permitting, I would welcome conversations on how to deal with the various oddities I found in principle; I'm not sure how to make their diversity fit well into the guidelines I have. Future tenure-track faculty in WID with more diverse interests will likely be grateful, if some of my experiences are considered.

   To give you a sense of the work I did, I attach all figures and the Integration Overview Statement I produced for my dossier.

2. **Almost all details related to DIR**
   This includes all entries any lab-notebook worthy of 'a great Wisconsin Experiment' should have. There are too many for me to write them up in any reasonable context. Doing so would go at the expense of writing Evolvix. Sorry, hard choice.

3. **A draft figure of how a DIR might fit into WID**
   This is easily generalized to any modern university; I'll likely draw such a figure when I am transforming the general points in this text about DIR into a draft publication. I have several nice ideas on how to do this, but no time for PowerPoint right now.

Appendix 0: Mini questions and practicalities I will bring up again as needed

A. HR questions about a ‘post-autoclaved pod world’

Current people in my group:

- **Seth** 10% but could get more any time.
- **Jane** (student, artist): She would like to continue to work with me and has indicated interest.
  My work on the Evolvix Giants (see attached) is in preparation for selecting what to draw.
  I hope she can draw the giants. She might have a bit of time this semester, but is mostly looking for after her graduation in Dec
- **Lynn** is a professional freelance editor who has started to help me with interactive writing (ca. half day)
- **Open position** for ca half a day of interactive writing support.
  Since Jocelyn left there didn’t seem the time to re-hire as I was constantly trying to ‘get it all done’ as urgently as possible. As soon as I can after completing this text, I should integrate my latest experiences into a revised job description and advertise.
- **How should I handle students interested in contributing?**
  Can I still accept some?
- **Participants for my NSF grant**
  I have funds for 2 teachers (‘participants’) in the original grant to help me make Evolvix lesson plans. Once I have a clearer plan after moving out of the Pod, I may have additional questions on how to make this work. This is only a heads up.

B. IT questions that will come up in a ‘post-autoclaved pod world’

Currently many of my critical IT needs are met by WID IT. As far as I can tell, the move does not require any immediate changes, however, some questions arise on the longer term.

This is a heads up and you may not need to get involved in any of this, as I can sort most of it out with WID IT. I will let you know if there is something that you would have to decide.

- **Two powerful servers in WID belong to my NSF grant**
  They are in the basement of WID. While in principle I can do anything I need with them right now, I have to clarify what I can or cannot do with them on the longer term. This may impact how much time I can invest in various options.
- **Two older servers in WID came from startup and were extended by NSF indirect**
  These have been serving various functional tests. They raise similar questions. I will need to assess first, what the possibilities are, before I have questions, first for IT, maybe later for you if needed.
- **Other WID IT services**
  Various virtual machines have been critical for running various infrastructure parts of my lab, including websites and version control servers. I will have to find out what options might exist, before I may have any questions for you.

C. FlyC16 questions on interdisciplinary diversity and authorship

Interdisciplinary research requires translation between at least two languages and can be fraught with confusion. In this FlyC paper I aim to develop approaches to address these problems. Similarly, defining ‘authorship’ can be complicated for interdisciplinary studies, as each discipline has its own emphases. **My questions in these areas would benefit from your input.**

Appendix 1: How stable is WID?

At construction time the answer for the building itself was “we build for 100 years of active use as a research facility.”

The reflections in the next Appendix on the nature of centers and departments might suggest that WID as an interdisciplinary research center at UW-Madison might live significantly shorter, if it runs out of money. In this it could follow the ‘Enzyme Institute’ that was successful for a long time. I doubt this affects the building, as UW-Madison certainly has provisions to repurpose the research space for other uses. Such a repurposing could happen, if the pendulum swings the other way, and the idea that interdisciplinary research is worth the investment falls out of favor. Modern science is not free from fashions that come and go in waves. The ‘systems ecology’ of the 1970s was a high funding priority and generated much excitement, but few hard results at the time. When people realized its problems were too complex for quick answers, they lost interest and found other topics to investigate. Comments about ecology a few decades later (not necessarily by ecologists) carried little of that excitement; on occasion, words like ‘soft science’ were used and often threw out the baby with the bath water (in my mind).

If WID does not find a way to systematically harvest the interdisciplinary research expertise developed by individuals in WID as they conduct their ongoing research, it will remain severely limited by the departmental risk-mitigation strategy traps I described. These could be severe enough to prohibit WID from meeting the very high expectations of the broader campus.

Enemies of WID on campus? The thought was first unthinkable to me. Sure, I had noted that expectations had become a bit high and of course WID is not perfect (nothing is); but why would someone not want to root for WID? Yet, that might not be the whole story – at least not for some people on campus, who have been in Madison longer than me. How do I know? Some years ago, someone surprised me with an obviously well-intended comment, saying “*I hope that WID will succeed.*” I was grateful for the good wish. As WID’s success was beyond question for me, I also asked what was meant. I then heard for the first and only time from anybody that “*many on campus hope that WID fails.*” I was too surprised to ask any more questions, but I kept wondering what it may mean. Hope is a powerful force that can become very destructive if misguided. I do not wish to blow this out of proportion; I’ve never heard a similar far-reaching statement again from anybody and I don’t think it should make a difference that while talking to me, someone else jokingly referred to “the $200M coffee shop.” A sample size of n=2 is not a good basis for defining the semantics of ‘many’ here (it is a surprisingly flexible way of saying ‘more than a few’, albeit without a clear upper limit short of ‘almost everybody’). Thus, it is not clear if my sample translates into a significant invisible percentage, if it includes decision makers, or if it simply does not matter. Maybe none of this is new to you. However, I am only writing this letter in the first place, because I think it is important that WID succeeds. If indeed sentiments like those above have been growing while you were not in Madison, there is a chance nobody wanted to surprise you (and others in the ‘WID orbit’ may not know if frequencies outside are different). As a result, near-invisible opposition to important WID initiatives might strike in strange ways at inopportune times and cost you precious time or opportunities to react. I wouldn’t want to go so far as to suggest that there is a con in the fox, but I can’t exclude it either. You know Madison culture much better than I do, so you will know what to do with this if anything. I would hate for WID to be starved to death in very polite and professionally appearing ways that are no less effective. I recall informal comments from David Krakauer about observations he made that could be interpreted that way.

Appendix 2: Why WID needs tenure to develop its full potential

De-*part*-ments have to build walls to stabilize and streamline their teaching mission.
Good reasons exist for why departments systematically bias themselves towards more homogeneity and stability. Most of these are grounded in their teaching mission. Before we look at stabilizing and streamlining mechanisms, here are a few examples to illustrate that the consequence, namely wall-building, can be seen in very diverse areas of academia:

- Genetics departments worry about their borders from biochemistry to ecology.
- English departments worry about where to draw the lines with journalism and communications.
- Computer science departments differentiate from math (where they originally came from); in the age of data science and strong computational work in other sciences, the worry becomes which areas of research and teaching should rather be handled by statistics and corresponding disciplinary science departments (in contrast to computing as a science that stands by itself).

The list is easy to continue. The amount of mental energy used for defining, upholding, defending, and moving those boundaries varies across departments, their life-history stage, and their context.

Yet, why the effort to build and keep those boundaries? At its core, the answer is in how to train the next generation of researchers. Everybody starts with zero knowledge at birth. Ignoring individual exceptions, there is only a limited speed for acquiring the skills necessary to build up academic expertise. Curricula are generally already overloaded, whether in K-12 education, at the undergraduate college level, or in graduate schools: experts rarely worry about how to fill any given course with relevant material; rather they worry, what they can cut out to reduce the cognitive load to realistic levels. The work of cutting is easy, if outdated knowledge can be *replaced* by updates. This can simplify learning when a confusing array of details is replaced by a simple elegant theory that is well tested and not excessively complicated. However, on other occasions, updating simply means to provide more fine-grained views or to fill-in blanks in a map as the cutting edge of research collects additional data and builds new theoretical and simulation models. In such cases, an updated curriculum requires hard choices, as days have only 24 hours for everybody, and there are limitations to how much can be squeezed into any given curriculum. In college, the solution to this crunch has increasingly become to streamline teaching into specialized degrees that present perspectives shaped by a department's disciplinary views, assumptions, methodologies, fundamental results, and the like. Such an organization into 'silos of knowledge' has the benefit of greatly accelerating communication and thereby research within communities of similar-minded scientists. Since nobody can know everything, the growing complexity of academic work makes it inevitable that the *universe of discourse of a university* will be broken into smaller parts that are ultimately managed by de-*part*-ments, which are sometimes grouped into colleges that share a school of thought.

Natural no-go zones. Irrespective of the particulars of where departmental boundaries are drawn at a given university, the very existence of such boundaries creates 'no-go zones': these areas of expertise exist conceptually, but investigating them is not currently supported by any department. They fall in the space in-between. A lack of support may not keep adventurous researchers from exploring such areas; however, sometimes a lack of support can imply opposition. Interdisciplinary research can easily find itself in such a no-go zone if a department feels the need to limit their faculty's research if it deviates too much from the departmental core discipline (e.g., by integrating too many aspects from other disciplines). The merit of such limits is easy to understand in many cases; yet a long tail exists where such decisions are much less clear and a department's felt need for more coherence can easily translate into prohibitive complications for research areas the department perceives to be outside of its remit.

Consequences for interdisciplinary research centers. Centers like WID, who have no choice than to work with departments, can thus find it complicated to maintain research programs that require the investigation of areas in departmental no-go zones. Thus, for centers like WID, the potential for interdisciplinary research innovation is *conceptually limited* in principle; practically, details are left to the mercy of how firmly a disciplinary department intends to guard its boundaries. Departments are systemically incentivized to limit consciously or unconsciously how much interdisciplinary research they might want to tolerate among their tenured faculty – in order to protect their stability, which is essential for a department's long-term teaching mission. Thus, the systemic bias of departments for sufficient homogeneity is not directed against interdisciplinary research itself. Instead departments are set up to select against any type of researcher or influence that reduces their stability too much. It is easy for interdisciplinary research centers to detect such blind spots. The administrative unit of a research center exists in modern universities to enable quick responses to research needs that can change on time-scales much shorter than relevant for the slow changes of teaching needs for departmental disciplinary degrees. Research centers, of course, have their own blind spot: they do not teach at all. Hence, research centers swap the effort departments spend on teaching for increased operational flexibility that allows them to use more diverse approaches for advancing research. In order to understand the efficiencies research centers can gain by developing innovative batching strategies, it is useful to consider the batching strategies that have made the departmental model for organizing research extraordinarily successful.[11]

Batching strategy: tenured faculty in departments stabilize its long-term teaching mission and efficiently ensure that teaching at universities stays reasonably up-to-date.
Stability is essential for reliably performing the key task departments have in their mission that research centers do not: teaching. Successful teaching pipelines need stability in order to fill, to get accredited, and to develop a system that allows students to find work. Creating and maintaining pipelines for running successful high-end degree programs requires many long-term investments to ensure a high degree of quality over the long term. Stability is enforced by reviewers from independent accreditation authorities. Thus, it seems fair that universities stabilize high-quality degree programs by encouraging their teachers to stay with them for the long term.

To base tenure decisions on the ability to conduct cutting-edge research turns out to be a remarkably efficient tool for updating teaching materials implicitly. Grouping tenured faculty with similar interest in departments responsible for running degrees is elegant and efficient:

- Long-term faculty will tend to develop long-term research programs that tend to move them to the cutting edge of research in their area.
- Such faculty tend to leverage their research expertise to update teaching materials, which thus tend to be more up-to-date and of a higher quality than if teaching is based on updates produced by non-experts with no cutting-edge expertise
- Thus, tasks are grouped in ways that ensure almost automatically, that teaching at universities stays reasonably close to the cutting edge – the expertise of leading researchers naturally trickles into their teaching (and onward from there).

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[11] Jerry A. Jacobs, "Disciplines and Interdisciplinarity in Research Universities", online draft of presentation at the National Research Council Meetings on Team Science, October 24, 2013.

This is a remarkably efficient batching strategy. Maintaining its efficiency requires little or no external pressure for keeping teaching up-to-date; leaders in their fields usually want to keep their teaching up-to-date anyway – assuming they get the time and job stability required to do so.

It works! This system of incentives is an efficient and versatile model for organizing academia. It has proven itself over centuries in western universities and supported a great expansion of new disciplines and degrees in the 20th century as the growth of knowledge resulted in more specialization and a narrowing of departmental interests, at least in some disciplines.

Other homogenizing forces in departments. As compelling as teaching is as a justification for the homogenizing stability and risk avoidance of departments, there are other reasons too. For example, cognitive consonance can cause groups to emerge, where 'like' likes 'like' (and all feel right – even though group-think merely perpetuates collective blind spots). Such reasons can make it difficult to increase the diversity in any closed group, even if there is no stability requirement. Unfamiliar disciplines can easily trigger irrational fears or cross-cultural misunderstandings that can break budding research links. Particularly clear examples are easily found in the numerous tensions created by disciplinary differences along the bio-math divide.

Departments and research centers serve fundamentally different purposes. Research centers in universities exist to facilitate timely research needs, which are typically funded externally. Since they do not have teaching missions as departments do, research centers are only as stable as their external research funding sources. These can fluctuate greatly as research needs can change rapidly. Research centers do not receive tuition money, a substantial source of stability for departments. Over the long term, therefore, research centers tend to have much higher rates of turnover than departments. Hence, it makes perfect sense, that departments can offer tenure, at least to some faculty, whereas research centers cannot.

Tensions. The fundamentally different missions of research centers and departments can result in conflicting risk-allocation strategies that can easily short-change either party, especially if they have very different sizes. There are few rules for how small or large departments or research centers can be. Thus, it is possible to have very small departments with tenured faculty and very large research centers (like WID), where faculty cannot be tenured. This has consequences for risk allocation with potential impacts on either the agility of research centers or the long-term stability of departments.

Allocating decision power and risk among departments and research centers. To improve the long-term stability of successful research programs, research centers often wish to offer their faculty tenure. If they exist within universities, they have to play by university rules, and these typically (and possibly exclusively) imply that faculty can only be tenured in departments. At least that seems to be the case for all interdisciplinary research centers within universities I am aware of. Yet, as discussed above, the tenure-type appointments controlled by departments are meant to ensure the long-term stability of teaching missions – a very different purpose from the reasons research centers might want to grant tenure. This can greatly complicate interactions between departments and research centers, if the latter aim to keep faculty-level scientists that serve an interdisciplinary mission, yet need to satisfy much more narrow tenure requirements optimized for stabilizing the long-term teaching mission in their home departments.

Who carries the risk? Tensions are likely exacerbated if departments sense that there is a chance that they will have to carry the risk for more daring interdisciplinary research projects that a center may want to support. If all goes well, there is never a problem. However, the definition of 'high-risk, high-reward' research is meaningless, if ways existed to certainly avoid the risks and always collect the rewards. The absence of clear definitions and reasonable backup strategies that actually allow for failure in predictable ways will either result in unpredictable circumstances for failure ('knowing after seeing') or lead to implicit hidden avoidance of risks if failure is unacceptable. Since it is difficult for others to predict the risks associated with a given research path for a given researcher, the real amount of risk entertained is easily modulated to much smaller risks by ‘picking low-hanging fruit’ in non-obvious areas. The resulting research output might appear even more impressive than if more new ground had been broken – yet it can be difficult to decide for those who have not tried to break new ground in that particular area. The particulars can be hard to pin down as scientists at the cutting edge of research usually only get there by developing a good intuition for the risks entailed by research questions in their area. This intuition can allow them to efficiently adjust the risks they are willing to entertain by modulating seemingly insignificant project details. This can change projects that start out as high-risk, high-reward into much less risky projects of more limited benefit. In these cases, the risks are carried by those who would have benefitted from the more ground-breaking research results that might have been found. Yet, since nobody will ever know, these risks do not appear on anybody’s balance sheet, whereas in reality they are carried by the next generation (‘those who do not benefit’). To minimize such risk avoidance by researchers or the organizations that employ them, it is important to consider the worst cases in more detail.

What if the leadership of a research center decides to send a faculty member paid by the center back to their tenure-home department? This scenario is useful to consider irrespective of detailed institutional arrangements about who continues to pay for the salary. In either case, there will be an unfair winner and loser, resulting in an overall loss of efficiency carried by the university as a whole and implicitly by funders of such arrangements.

- **If the center continues to pay** a faculty that from now on contributes only to the home department, then the center will have lost resources; if this happens repeatedly, the center may lose its ability to pay any faculty and may have to close. It may look natural, the research at this center ‘has run its course’, but that does not necessarily make it natural. In particular, there is a possibility that departments may have biased the hiring and tenure decisions of such a faculty member in ways that may not be entirely unrelated to the reasons that have made this faculty member less useful for the interdisciplinary research in the center.
- **If the department starts to pay,** then a center might easily endanger the stability of collaborating departments. If centers hire faculty for high-risk, high-reward research ideas or simply ask them to work on such projects, yet off-load faculty with less than spectacular results to departments, then departments might have to scramble to find the funds to pay for an extra faculty salary. Any responsible departmental leadership with a view to departmental needs for stability will of course not let it come to such surprises. Instead this eventuality will have been figured into hiring and tenure decisions and all the advice a new faculty member will receive in this department. The goal of a clever department will therefore be to ensure that any new faculty member sufficiently conforms to the department’s expectations as this will minimize the disruption caused in case this faculty member would have to be fully integrated into the department’s teaching mission.

In either way, it is easy to see how the fun and efficiency of interdisciplinary research in a center can be crippled by the competing objectives of keeping the center efficiently researching questions that might be of little interest to a department and guaranteeing a department’s stability by ensuring all its tenured faculty are sufficiently homogeneous to blend well into the various teaching tasks a department has.

Thus, regardless of who is paying, one or both parties are easily short-changed if the power to make decisions is separated from the responsibility to carry the risks.

These problems cannot be solved by ignoring or postponing the exploration of case-by-case solutions as necessary. The resulting lack of clarity would require diligent departments to plan for the worst – with the same devastating consequences for the diversity of the interdisciplinary research that can be supported by the research center in question. There is no solution to this dilemma without giving centers like WID the power to make tenure decisions in support of particular strands of interdisciplinary research deemed important by a center's leadership; a center will only be able to deliver its full potential if it can provide the freedom tenured research faculty need for engaging with the questions necessary, regardless of disciplinary boundaries.

This has broad implications for how to best organize interdisciplinary research elsewhere. Centers for interdisciplinary research are not typically given the authority to make tenure decisions by their universities. This analysis is independent from the particulars of how other universities may have separated these risks from the abilities to make tenure decisions. The only feasible solution for ensuring that research centers can make the best hiring, mentoring, and tenure decisions in the interest of interdisciplinary research is to: allow centers to make tenure decision.

See other parts of this discussion for how research centers might obtain the ability to grant tenure without up-ending much the basic wisdom of how modern universities are organized efficiently.

Appendix 3: Departments in WID that would limit its diversity

What type of department could possibly be worth the effort of setting it up in WID?
As noted by a recent comparison of the breadth and success of science found within disciplinary departments and in various interdisciplinary research centers, the author reaches the surprising conclusion that **interdisciplinary research centers tend to have a narrower scope than departments**.[12] I was first surprised by this conclusion, but did not have to think of many interdisciplinary centers, in order to agree, at least in many cases.

Why? As long as disciplinary researchers within a department stay within their disciplinary boundaries, they have vast flexibilities in choosing and adjusting their area of research. In many departments this amounts to large degrees of freedom that can easily be explored without the need for much bureaucratic overhead or complicated justifications. This freedom allows for much diversity within departments.

Yet, such freedom is not as easily found in interdisciplinary research centers, as they need to justify their specific research purpose more precisely. Thus, many of these centers – unsurprisingly – either focus on a narrow area where a couple of disciplines intersect, or on a specific problem, model, system, or question. If large grants and corresponding justifications are necessary, interdisciplinary research starts to resemble a specific puzzle that invites some disciplines to contribute their pieces to the solution desired by a funding agency or faculty member in that area.

Maybe agreeable intersections in WID are likely broad enough to merit their own department.[13] However, for conceptual reasons I doubt it would be worth the effort to determine which of these are best developed into a department. The need to start with some combination (and therefore at least for now exclude all others) would create a very specific department that could still not serve all other combinations which are rightfully represented in WID.

In contrast, a Department for Interdisciplinary Research (DIR) is free from such conceptual limitations.

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[12] Jerry A. Jacobs, “Disciplines and Interdisciplinarity in Research Universities”, online draft of presentation at the National Research Council Meetings on Team Science, October 24, 2013.

[13] Options are plenty in old WID themes, new hubs, or shared topics of interest, such as quantitative biology. However, whether these are indeed broader than related departments or not, depends on their precise definitions; it does not appear certain to me that such interdisciplinary combinations would indeed be broader. However, what *is* certain is that many ways exist of defining such interdisciplinary departments and that *all* of them will *exclude some* important work that could equally well have ended up in this interdisciplinary WID department if it had only been defined in a different, equally justified way that would have allowed for the necessary intersection. Thus, it makes no sense to me to further explore such rather narrow ideas of defining a WID department for purposes of giving WID the power to grant tenure. **Inconsistent and arbitrary definitions are harmful.** I’ve seen in 2007 after entering current systems biology how much unnecessary confusion was caused by the refusal of many ‘system biologists’ to define systems biology (nurturing the cynic suspicion of some that systems biology was a mere ploy to fund some groups at the expense of others). The last thing WID would need is such a round of cynicism caused by unnecessarily narrow definitions of interdisciplinarity in WID that would also complicate potential new collaborations with disciplines accidentally omitted from one definition but not from another. This is where my best ideas on potential departments would have ended for most of my time in WID; unsurprisingly I have also never heard any serious discussion of such more specialized departments. I think the reason is that none of these specialized ideas make much sense. Then DIR showed up.

Appendix 4: Credibility and reasonability in an interdisciplinary context

Attacks on researcher credibility are easy to launch across disciplinary boundaries and unnecessarily costly within academia and beyond. Such friction could be reduced by a DIR. Several types of such attacks matter in an interdisciplinary context, either because of their detrimental consequences in terms of severed lines of communication or because of self-censorship aiming to avoid such consequences, albeit at the cost of significant side-effects.

1. Department – tenure candidate. An unnamed population geneticist at a distant institution once mentioned in a private meeting with another researcher that departments who dislike a tenure-track candidate for 'cultural' reasons tend to discredit the science of the candidate. Such 'cultural' reasons can obviously be very diverse and likely live in a complex grey area between valid concerns and unfair judgements; they can certainly include the disciplinary match between the work of a candidate and the disciplinary culture of a department. A DIR could assist by developing strategies for reducing unnecessary conflicts and assist departmental implementation.

2. Interdisciplinary researcher – disciplinary expert from a new discipline at first meeting. Entering a new discipline can be daunting, even for seasoned interdisciplinary researchers: in many important respects doing so is the decision to start again as an undergraduate (except for shared expertise like statistics). Like new undergraduates, researchers from distant disciplines have to learn many basics, yet they rarely have the luxury of actually taking the time to work through the basics like undergraduates do. Thus, they have to accept the risk of never knowing which basic tenet of the new discipline they may violate as they move in this new space.

This can quickly lead to situations, where **credibility with an expert from another discipline can be lost rather quickly by asking the 'wrong' questions** that betray gaps in the disciplinary knowledge that would be embarrassing for a disciplinary insider. There remains work to be done for improving how to handle this. It is of course often possible to hide gaps in knowledge and thereby preserve one's professional credibility. If this option is always chosen, learning tends to be very slow as basic assumptions are rarely spelled out (as experts would do for beginners).

However, experts often have an extraordinary grasp on assumptions that their answers can be so much more illuminating for an expert in another field than answers to the same question typically provided by other beginners. Hence, **it can be worth 'risking reputation' to hear the basic explanations from an expert in the area. Many have found that learning is maximized by asking exactly these 'embarrassing' questions,** thereby admitting vulnerability, and asking for help. Neither of these is usually a problem if the other expert has some experience in communicating across disciplinary boundaries. However, not all disciplinary scientists have the opportunity to develop the necessary skills. As a result, the professional credibility of the person asking can be damaged rather quickly. **This problem can be exacerbated by stereotypes that amplify perceived notions of 'clever' or its opposite. The math-bio divide can be particularly vicious in that respect and certainly merits special DIR attention.**

For example, **math-phobia** was not invented by students too lazy to complete their homework; it is a major problem that needs serious attention or else it will continue to severely limit quantitative analyses in biology.

3. Expert to expert, even in the same discipline. When experts in their area meet, especially if they do not know each other from previous interactions, then the ensuing interactions can create credibility problems if not handled well. The problem is best described in the words of John Kenneth Galbraith[14]:

> ***"A professor is judged by his or her peers. These are omnipresent, always looking for scholarly competence and perception, or, more poignantly, their absence. So even a full professor...must always stand at attention.... From this heightened sensitivity to scrutinizing peers comes a certain dulling of personality. No one can now afford to seem eccentric. Nor is the judgment above reproach. Professors considering and selecting others for promotion define excellence, perhaps inevitably, as that quality of mind and work that most resembles their own."***

He was talking about trends of how academia at Harvard changed over some time in the 20th century. Such a climate poses serious problems for interdisciplinary research dialogues, where the absence of some scholarly competence is a given.

It can be surprising to enter academia with a passion for learning and find that its most educated members make learning unnecessarily difficult for themselves. If WID aims to encourage *wid* and the implementation of *WId* projects that regularly require interdisciplinary collaborations, then approaches for maximizing the speed of learning and minimizing side-effects such as loss of professional credibility are clearly beneficial. Once developed, teaching such approaches as part of a DIR curriculum is likely to be met with broad interest from both students and their prospective employers. For a DIR to develop and teach less ruinous ways of communication is clearly also of internal interest to WID to reduce the frequent collaboration calamities across the math-bio divide.

4. More threats to apparent credibility. Also, collaborative lines of communication can be easily threatened by other cultural factors, such as

- incomplete cultural transitions (e.g., moving across countries; not aware of local customs),
- first-generation student background (e.g., some assumptions taken as given by others may not be shared),
- medical issues that can lead to unusual communication patterns,
- training in certain unusual disciplinary views; for example, computer security experts have sometimes been described as 'different'; unsurprisingly, they need to take a very different and unusual perspective when testing software (e.g., celebrate it as progress, when a new problem is found, since they know that the absence of evidence for problems is in most cases not evidence for absence),
- Higher levels of openness about the limitations of one's own work can easily be mis-interpreted as admissions of excessive weaknesses by other researchers who do not tend to question their own work at great length and thoroughness.

This list goes on. Culture is of course hard to shape; yet, it is not impossible in professional contexts. Airlines had to learn how to train junior pilots to clearly, professionally, and respectfully communicate navigation errors to senior pilots in cultures where respect for a senior person would usually imply that errors are not pointed out. Unfortunately, an airplane had to crash into a mountain, before the need for such training was recognized.

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[14] John Kenneth Galbraith (1981, pp 58-60) as cited in a Google Book by someone else.

It is not clear, what would have to happen in science in order to motivate the adoption of clearer communication standards; the needs are in many ways obvious. However, it may be possible, that suitable standards in science have not yet been developed to provide sufficient simplicity, nuance, and clarity in order to make adoption reasonable.

5. Broader implications. There are millions of scientists around the globe, but most citizens are not scientists in the sense of being professionally paid for working in research full time. However, a large fraction of the general population has or had some contact with science which left an impact of some sort. Struggles to test the quality of news and to develop systems for reducing the amount of fake-news are ultimately also about communicating or preserving credibility across lines of communication. It is not clear, whether systems developed for communicating more clearly in science could work in a broader context; however, it might be safe to say that if scientists cannot solve the problem of robust communication among themselves for learning in the context of interdisciplinary research, then the chances of finding a more general solution for a broader population may be even worse.

Appendix 5: A Legacy Draft of Table of Content for Frontmatter of Tenure dossier

In mid-Summer 2018 I thought a collection of texts like these may form a frontmatter bundle that presents background information on how I transformed my work at WID into a more classical departmental tenure dossier. It was meant to assist reviewers by providing a more rounded overview of the unusual work I did, the progress I made in my view, and my perspective on the challenges I faced. Then it became increasingly clear that it would take too long to write all this; also, it would likely only end up collecting imaginary dust on hard drives. To transform lessons, which I learned into something more relevant for WID, I distilled down their essence for WID's interdisciplinary mission in the main text to which this appendix is associated, omitting many details I observed and considered to be symptoms of the larger forces at play.

Other references of interest include [12-16, 18, 35, 39, 42, 44, 52-54, 58-91]

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A. My Incomplete Tenure Dossier

or

The remains of my attempt to fit a shepherd-dog into a shoebox

This material are the core pages of my tenure dossier in its current state. I tried to represent my diverse research in a way that conforms to the expectations of the Laboratory of Genetics, my home department. I had much help from Nicole in figuring out what the precise expectations of my department were and I tried to meet them as well as I could under my given circumstances.

*There is much more that could be said about the details of my struggles, but in the end, I think that the 'felt need' to conform (more? exclusively? immediately? sufficiently?) to particular disciplinary expectations created much confusion at my end. I worked as hard as I could towards meeting my department's expectations, albeit without at the same time dropping the interdisciplinary work that motivated me in the first place to come to Madison and that I felt some mandate for by virtue of being in WID and by being funded by an inherently interdisciplinary NSF Career Award from the '*Advances in Biological Informatics*' program. My productivity was reduced by the confusion generated from these conflicting expectations and many context switches, some resulting from this confusion, some from the normal pressures of academic life (in addition to more personal causes that took a cumulative toll).*

I realize that nobody would have stopped me from acting as a 'disciplinary population geneticist' by ignoring all interdisciplinary ideas, hints, and questions. However, I still feel strongly, that this would not have been in the best interest of research in genetics, since genetics – like many modern areas of biology – has much to gain from effectively integrating modern IT tools into its research and teaching.

Hence, I perceived a conflict between the narrower disciplinary expectations of departments (incentivized to maintain homogeneity and defend their borders) and the contrasting need to integrate many interdisciplinary perspectives in order to address the pressing problems of our time. This conflict – or so I have come to conclude – was more important for the final outcome than my other shortcomings.

1. **Background** statement (and **Fig.0**: overview of the disciplines I draw from)
2. **Integration** statement (and **Fig.1**: ecological forecasts; see **Poster (a)** for larger print)
3. **Research** statement (and **Fig.2**: game theory in Evolvix; **Fig.3**: biouncertainty measured)
4. **Teaching** statement (and **Fig.4**: influenza model from students in my course)
5. **Outreach** statement (and **Fig.5**: design flip method for developing new languages)

The numbering of headings below follows the biological division template of UW-Madison.

Introducing **my 4 2 representative publications** and 10 biased ways of selecting them

Proxy evidence: Given the enormous systemic uncertainties in how to appropriately report my '**evidence for establishing an independent research program**', please accept my most recent CV as a proxy for the more usual lists of papers, grants, and more that I am not sure how to compile appropriately.

Tales from Falling Through a Rabbit Hole into the Interdisciplinary Wonderland of

Advancing Evolutionary Systems Biology

by

Laurence 'Lion' Loewe
Principal Investigator

First external hire to the WID Faculty
at the **Wisconsin Institute for Discovery** (WID)
Asst Professor in the **Laboratory of Genetics** (LoG)
University of Wisconsin-Madison (UW-Madison)

presenting a tentative incomplete draft

Tenure Dossier

prepared (as good as possible) according to the formal instructions described in the
University of Wisconsin-Madison Faculty **Division of Biological Sciences Guidelines** for
Recommendations for Promotion or Appointment to Tenure Rank, as effective December 2017,
with specific additions as deemed necessary for covering the interdisciplinary nature of this work

enabled by the generous support of WID *and* LoG *at* UW-Madison,
National Science Foundation (NSF) program 'Advances in Biological Informatics',
National Institutes of Health (NIH) support for General Medical Sciences (NIGMS),
the hard work of researchers in my group, and the dedication of many ***Evolvix.org/thinkers***

2018-10-05
version 0 release 3 patch 0

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5. Background Information on the Candidate

5A. Name

Laurence 'Lion' Loewe

5B. Formal Education

High school: *Gymnasium Fridericianum Erlangen,* 1988. German *'Abitur'*

Jugend forscht Competition, 1987, 1988, 1989, 1990, 1991
These annual formal competitions are an important known contributor to the science education in Germany; they are similar to the *Science Talent Search* in the US. For 5 years I conducted extensive, self-directed experimental research in chemistry and physics on the impact of measures of electric discharges on organic compound production in Miller-Urey chemical evolution experiments. I produced annual reports for five competitions and my work was supported by scientists from diverse departments across the University of Erlangen, Germany. This was a great opportunity for learning how to work between disciplines and realizing the importance of quantifying measurement errors and lower detection limits.

Public service: fulfilling a mandatory civic duty at that time in Germany, 1988-1990

College degree: *Diplom Biologe* (equivalent to MSc in molecular biology), 1990 - 1995
University of Konstanz, Germany; including 9 months of experimental lab work in biochemistry to support my thesis that conducted site-specific mutagenesis in the active center of human Medium Chain Acyl-CoA Dehydrogenase and measured its effect on catalytic activity.
Advisor: Ihab Rasched, research in biochemistry

Graduate work: *Dr. rer. nat.* (equivalent to Ph.D; *magna cum laude*), 2002
Microbial Ecology Group, Department of Biosciences, Technical University of Munich, Germany.
Thesis title: "*Evolutionary bioinformatics: predicting genetic stability of asexual genomes by global computing*." Advisor: Siegfried Scherer, research in molecular biology, microbiology

Postdoctoral Research Associate in Theoretical Population Genetics, 2003 – 2006
Institute of Evolutionary Biology, University of Edinburgh, Scotland, UK
Advisors: Brian Charlesworth, Deborah Charlesworth, both: research in evolution, population genetics

Lectureship in Evolutionary Genetics, Sabbatical Replacement for Nicholas H. Barton, 2006-2007
Institute of Evolutionary Biology, University of Edinburgh, Scotland, UK
Advice came from Andrew Leigh Brown, Nicholas H. Barton, Peter Keightley,
Deborah Charlesworth, Brian Charlesworth, and others at that institute.

Postdoctoral Research Associate in Process Algebra Modelling and Quantitative Analysis, 2007 – 2010
Centre for Systems Biology at Edinburgh, School for Biology, University of Edinburgh, Scotland, UK.
Laboratory for Foundations of Computer Science, School for Informatics, University of Edinburgh, UK.
Advisor: Jane Hillston, research in stochastic process algebras and modeling, theoretical computer science

5C. Positions Held

2011-01-07 to present	Assistant Professor of Medical Genetics, Laboratory of Genetics, School for Medicine and Public Health (SMPH); Wisconsin Institute for Discovery, University of Wisconsin-Madison, USA.
2010-09-22 to 2011-01	Visiting Assistant Professor. Laboratory of Genetics, SMPH, University of Wisconsin-Madison, USA.
2006-10 to 2007	Lecturer in Evolutionary Genetics (for that academic year) Institute of Evolutionary Biology, University of Edinburgh, Scotland, UK.

2003-02 to 2003-04 Visiting Scientist, IWR Technical Simulation Group,
Interdisciplinary Centre for Scientific Computing,
University of Heidelberg, Germany.

Secondary affiliations at University of Wisconsin-Madison

2011 to present	Permanent Faculty Member	J. F. Crow Institute for the Study of Evolution
2010 to present	Faculty	Wisconsin Institute for Discovery

5D. Honors and Awards

2017-02-06 **Review selected:** Encyclopedia of Evolutionary Biology (2016), 2132 pages.
When this 8-volume reference work was honored at the PROSE Awards 2017, my chapter on 'Systems in Evolutionary Systems Biology' and its 22 pages were chosen in full to promote this work by offering a free download at this URL:
URL: scitechconnect.elsevier.com/encyclopedia-evolutionary-biology-wins-prose-award/
Invited & reviewed by Hiroshi Akashi, it gives the first precise definition of EvoSysBio.

2012-06 to 2019-05 **NSF ABI CAREER**: Faculty Early Career Development Award,
NSF Proposal Number 1149123, entitled "*Modeling made easy: Extending systems biology modeling approaches to genetics and ecology*"
is the new end date, as the 2nd No-Cost-Extension has now been granted.

2005 ***Best Poster Prize***
"BioSysBio '05: Bioinformatics and Systems Biology Conference", Edinburgh, UK.
My first use of the words "Evolutionary Systems Biology"

1991 ***'Jugend forscht Landeswettbewerb', Second place in chemistry***
Stuttgart, BW, in statewide competition. Germany's *Jugend forscht* foundation supports research by young people. It is similar to USA's *Science Talent Search* by *Westinghouse, Intel*, and now *Regeneron*. My paper compared the yield/energy for three types of high voltage discharges in primeval atmospheres, summarizing results from the prior five years of experiments.

1990 '*Jugend forscht Regionalwettbewerb'*, Erlangen, BY, regional competition, chemistry.
1989 '*Jugend forscht Regionalwettbewerb'*, Erlangen, BY, regional competition, physics.
1988 '*Jugend forscht Regionalwettbewerb'*, Erlangen, BY, regional competition, chemistry.
In these papers I developed a quantitative approach for testing my first-year intuition that more powerful discharges were less productive than those driven by less electrical energy, which was confirmed. I reported increasing refinements of different experimental aspects. I built a larger plasma discharge device in the lab of a local research group in high-voltage discharge physics; I quantified the high-voltage discharges in my experiment using self-written code for analyzing the high-speed discharge currents that I measured in my three different devices with instrumentation from the same institute; I improved blank tests, purification procedures, chromatography and other chemical detection methods. This work was entirely self-directed and supported by gifts in kind, and advice as needed from industry sources and scientists in various university departments in my home town, mostly Physiological Chemistry, Organic Chemistry, Experimental Physics, all University of Erlangen, Germany.

1987 *Third place in chemistry*, '*Jugend forscht Landeswettbewerb'*,
München, BY, statewide competition; I won an internship at the German Cancer Research Center, Heidelberg. My paper focused on the significance of lightning in primeval atmospheres for chemical evolution by replicating 'Miller experiments' and adding rain to the setup to vary the conditions where the lightning occurred.

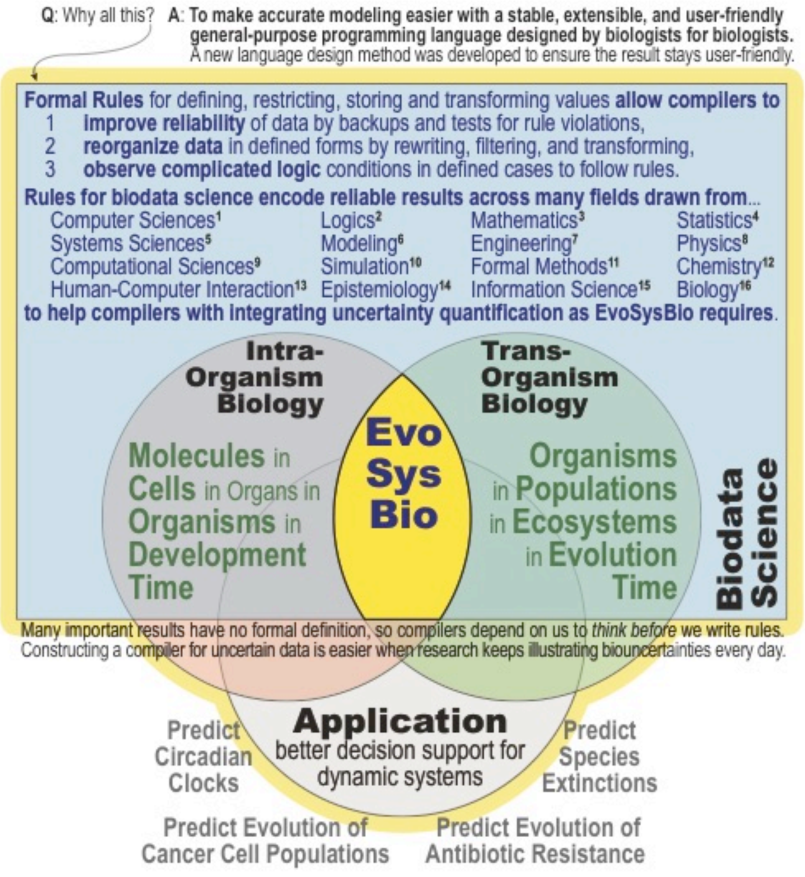
5E. Society Memberships

2012 to present	AAAS	American Association for the Advancement of Science
2005 to present	ESEB	European Society for Evolutionary Biology
2018 to present	Force11	Force11.org
2016 to present	GSA	Genetics Society of America
2005 to present	GenSoc	Genetics Society of Britain
2018 to present	ISB	International Society for Biocuration
2016 to present	NYAS	New York Academy of Sciences
2013 to present	SMBE	Society for Molecular Biology and Evolution
2011 to present	SSE	Society for the Study of Evolution

5F. List of disciplines shaping my interdisciplinary interests[15]

Fig.0 lists the various disciplines I draw from, and on occasion may contribute to, including how some of them are linked. Without building on the pioneering work of researchers in many diverse areas that belong to these disciplines, it would be impossible for me to contemplate, let alone seriously propose the research program I describe in the other statements.

Fig.0 List of disciplines that shape my interdisciplinary interests and enable much of my work. EvoSysBio can be seen as *intersection* or as *union* of the domains it connects; both views have their merits. Biodata science is intended to lift the capabilities in reproducible computing and uncertainty quantification to the level required for more involved EvoSysBio analyses. To contemplate the wide range of relevant topics, I had to leverage diverse research in areas that belong to the disciplines listed above. While I had always been broadly interested, from 2014 onward new dimensions were added much faster as I learned how to write a general compiler.



Q: Why all this? A: **To make accurate modeling easier with a stable, extensible, and user-friendly general-purpose programming language designed by biologists for biologists.** A new language design method was developed to ensure the result stays user-friendly.

Formal Rules for defining, restricting, storing and transforming values **allow compilers to**
1 **improve reliability** of data by backups and tests for rule violations,
2 **reorganize data** in defined forms by rewriting, filtering, and transforming,
3 **observe complicated logic** conditions in defined cases to follow rules.

Rules for biodata science encode reliable results across many fields drawn from...
Computer Sciences[1] Logics[2] Mathematics[3] Statistics[4]
Systems Sciences[5] Modeling[6] Engineering[7] Physics[8]
Computational Sciences[9] Simulation[10] Formal Methods[11] Chemistry[12]
Human-Computer Interaction[13] Epistemiology[14] Information Science[15] Biology[16]
to help compilers with integrating uncertainty quantification as EvoSysBio requires.

Many important results have no formal definition, so compilers depend on us to *think before* we write rules. Constructing a compiler for uncertain data is easier when research keeps illustrating biouncertainties every day.

---

[15] This section is neither required nor prohibited by the UW-Madison guidelines for the biological division, as of Dec 2017. I felt that this overview helps to present a more well-rounded overview of my background as a whole.

6. Summary Statement on Integration of Activities

Fig.1 is final, text is refined Refs to be inserted

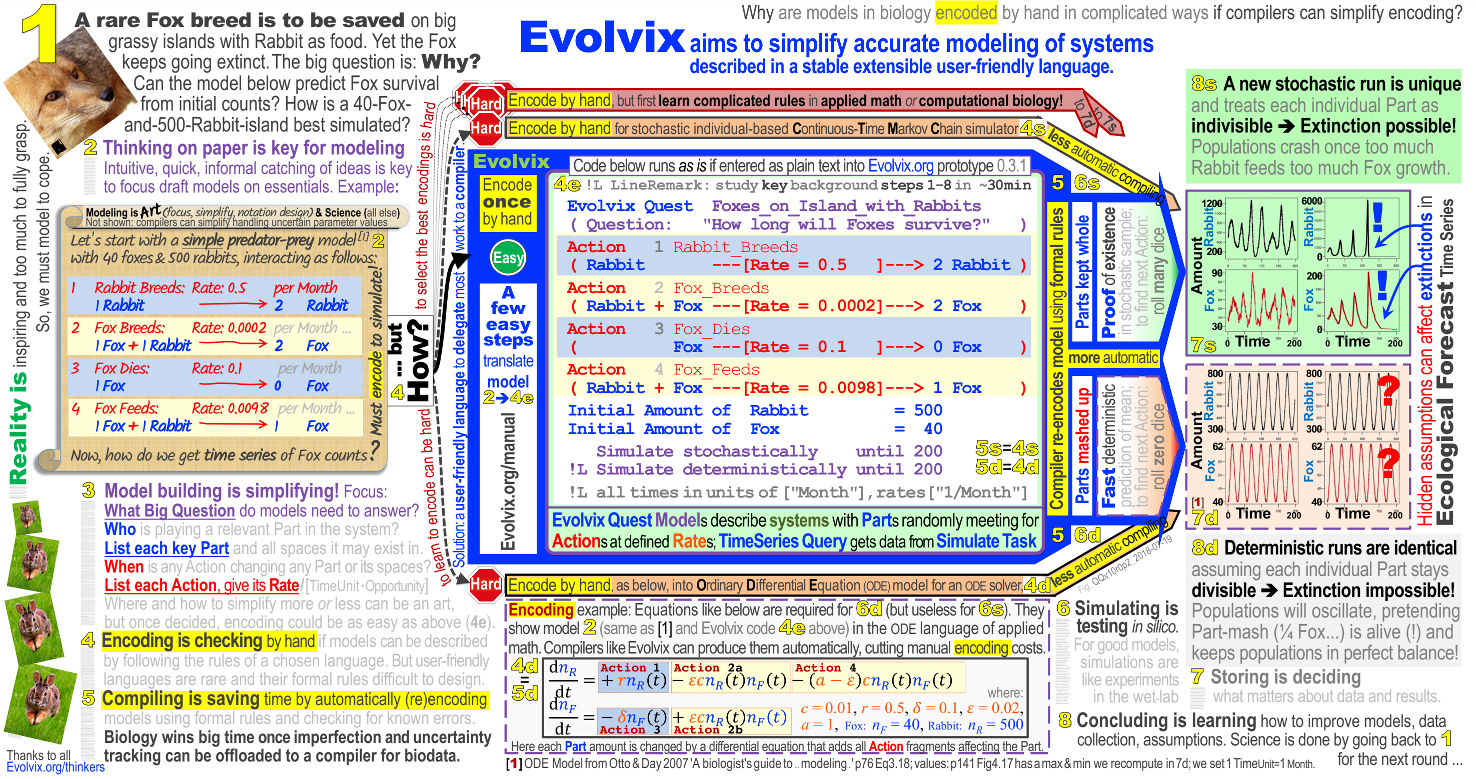
Simulations in biology unify my work. I improve their accuracy, clarify their meaning, and develop a user-friendly modeling language with growing functionality that simplifies reproducible modeling for both experts and beginners. To meet their needs, I integrated my *Research*, *Teaching*, and *Outreach* into a method for designing an architecture to stabilize this language on the long term as I work to personalize medicine and advance evolutionary systems biology.

I integrated diverse activities to improve the accuracy of *in silico* biology and make simulations more accessible to a broad biological audience. My research focuses on improving forecasts of evolution in diverse systems, [o2] including antibiotics resistance, cancer cell populations, potential species extinction [30] and cooperation. [29] Funded by an NSF Career Award, I created a new programming language called **Evolvix** to simplify modeling of systems in biology. [W1,26] To accelerate analyses, I selected accurate mathematical modeling frameworks to vary important assumptions and automated composing the model-specific input they require for simulating time series (Fig.1). My background in non-computational biology helps me to anticipate the needs of wet lab colleagues interested in modeling a system they study. Evolvix offers my colleagues a way to model their systems without the need to write ordinary differential equations or become computational biologists. Like people who drive cars that they do not have to build, biologists can thus focus on exploring models of their systems by using a compiler like Evolvix that automates most mathematical technicalities. I have been using Evolvix since 2013 in my course, research and outreach. [Ref] Evolvix helps students grasp biological concepts, lets interested 4th graders explore the model in Fig.1, and facilitates research in my group by automating tedious tasks. [26] I have built research models in diverse areas and have been leveraging this diversity to define concepts for Evolvix that are broadly applicable. To make modeling more user-friendly, I developed a new method for language design with outreach at its core (Fig.5). [28] As I assist users with their needs, I see their struggles and use these observations to improve the clarity and user-friendliness that I also need for my research in the long term. Students, collaborators, and outreach participants ask questions that are not limited by trained assumptions and have enriched my research in surprising ways. Integrating my research on abstract modeling concepts [Ref] with my outreach to potential users [Ref] for developing a stable user-friendly syntax pays off for teaching, [Ref] which in turn feeds my research [Ref] and outreach. I found that lasting extensions to Evolvix require a tight integration of all three lines of my work and sufficient time for review.

Fig.1: **This modeling panorama** shows **how Evolvix can accelerate and deepen biological thought** by moving busywork in modeling to a compiler. Experimental biologists often build mechanistic models in their minds. Evolvix assists by obtaining interpretable time series forecasts from a user-friendly syntax that is re-encoded (compiled) into two mathematical modeling formalisms shown below. Here a *hypothetical ecology* illustrates **8** steps in a modeling cycle. The textbook [1] result in step **7d** (via 5d,6d) is extended in **7s** (via 5s,6s) by recompiling to a formalism that treats individuals as indivisible, thus allowing extinctions to occur. **Warning**: easy to read in **over ~25min** or twice (tested), but text **may fry a brain in a hurry.**

Imagine, as if driving a car, biologists can rely on **a friendly compiler for translating** ideas about how a system works into simulations that predict observable time series. Imagine, such a compiler turns **readable statements** about a system's known biology, open questions, and remaining wiggle room **into** the **mathematics** required **for simulating** models. Such a compiler is rocket fuel for biology. It can explore many alternative models **to reduce guesswork in** planning **experiments** by calculating how much a potential measurement may contribute to testing some hypotheses of interest.

Biologists like modeling – **if only encoding were easier!** 100,000s of informal models published each year **can get a quantitative edge**, once modeling tools become easier to use and deal better with biouncertainty. So now, about **~99% of models built in biology are never simulated.** Example: SBML.org, one leading approach since 2003, lists 290 tools, has ~1650 published models in its BioModelsDB (rough avg. ~5.7 models/tool/15yr or ~120/yr). Too many tools?



Why are models in biology encoded by hand in complicated ways if compilers can simplify encoding?

Evolvix aims to simplify accurate modeling of systems described in a stable extensible user-friendly language.

1 **A rare Fox breed is to be saved** on big grassy islands with Rabbit as food. Yet the Fox keeps going extinct. The big question is: **Why?** Can the model below predict Fox survival from initial counts? How is a 40-Fox-and-500-Rabbit-island best simulated?

2 **Thinking on paper is key for modeling** Intuitive, quick, informal catching of ideas is key to focus draft models on essentials. Example:

Modeling is Art (focus, simplify, notation design) & Science (all else)
Not shown: compilers can simplify handling uncertain parameter values

Let's start with a simple predator-prey model [1] with 40 foxes & 500 rabbits, interacting as follows: **2**

1	Rabbit Breeds:	Rate: 0.5	per Month		
	1 Rabbit	→		2	Rabbit
2	Fox Breeds:	Rate: 0.0002	per Month ...		
	1 Fox + 1 Rabbit	→		2	Fox
3	Fox Dies:	Rate: 0.1	per Month		
	1 Fox	→		0	Fox
4	Fox Feeds:	Rate: 0.0098	per Month ...		
	1 Fox + 1 Rabbit	→		1	Fox

Now, how do we get time series of Fox counts?

Must encode to simulate! ... but **4** How?

3 **Model building is simplifying!** Focus:
What Big Question do models need to answer?
Who is playing a relevant Part in the system?
List each key Part and all spaces it may exist in.
When is any Action changing any Part or its spaces?
List each Action, give its Rate/[TimeUnit*Opportunity]
Where and how to simplify more *or* less can be an art, but once decided, encoding could be as easy as above (**4e**).

4 **Encoding is checking** by hand if models can be described by following the rules of a chosen language. But user-friendly languages are rare and their formal rules difficult to design.

5 **Compiling is saving** time by automatically (re)encoding models using formal rules and checking for known errors. **Biology wins big time once imperfection and uncertainty tracking can be offloaded to a compiler for biodata.**

Thanks to all Evolvix.org/thinkers

Reality is inspiring and too much to fully grasp. So, we must model to cope.

to select the best encodings is hard
to learn to encode can be hard
Solution: a user-friendly language to delegate most work to a compiler

Hard Encode by hand, but first learn complicated rules in applied math *or* computational biology! to 7d to 7s

Hard Encode by hand for stochastic individual-based Continuous-Time Markov Chain simulator **4s** less automatic compiling

Evolvix Encode once by hand Easy A few easy steps translate model 2→4e Evolvix.org/manual

Code below runs *as is* if entered as plain text into Evolvix.org prototype 0.3.1

4e
```
!L LineRemark: study key background steps 1-8 in ~30min
 Evolvix Quest  Foxes_on_Island_with_Rabbits
 ( Question:   "How long will Foxes survive?"    )
 Action    1 Rabbit_Breeds
 ( Rabbit        ---[Rate = 0.5   ]---> 2 Rabbit )
 Action    2 Fox_Breeds
 ( Rabbit + Fox ---[Rate = 0.0002]---> 2 Fox    )
 Action    3 Fox_Dies
 (              Fox ---[Rate = 0.1   ]---> 0 Fox    )
 Action    4 Fox_Feeds
 ( Rabbit + Fox ---[Rate = 0.0098]---> 1 Fox    )
 Initial Amount of  Rabbit          = 500
 Initial Amount of  Fox             =  40
    Simulate stochastically    until 200
 !L Simulate deterministically until 200
 !L all times in units of ["Month"], rates ["1/Month"]
```

5s=4s
5d=4d

Evolvix Quest Models describe systems with Parts randomly meeting for Actions at defined Rates; TimeSeries Query gets data from Simulate Task

5 **6s** Compiler re-encodes model using formal rules
Parts kept whole
Proof of existence in stochastic sample; to find next Action: roll many dice
more automatic
Parts mashed up
Fast deterministic prediction of mean; to find next Action: roll zero dice
5 **6d**

Hard Encode by hand, as below, into Ordinary Differential Equation (ODE) model for an ODE solver, **4d** less automatic compiling

Fig. QQv10r0p2_2018-07-19

Encoding example: Equations like below are required for **6d** (but useless for **6s**). They show model **2** (same as [1] and Evolvix code **4e** above) in the ODE language of applied math. Compilers like Evolvix can produce them automatically, cutting manual encoding costs.

4d = **5d**

$$\frac{\mathrm{d}n_R}{\mathrm{d}t} = \underbrace{\overset{\text{Action 1}}{+\, r n_R(t)}}\; \overset{\text{Action 2a}}{-\, \varepsilon c n_R(t) n_F(t)}\; \overset{\text{Action 4}}{-\,(a-\varepsilon) c n_R(t) n_F(t)}$$

$$\frac{\mathrm{d}n_F}{\mathrm{d}t} = \underset{\text{Action 3}}{-\, \delta n_F(t)}\; \underset{\text{Action 2b}}{+\, \varepsilon c n_R(t) n_F(t)}$$

where: $c = 0.01,\ r = 0.5,\ \delta = 0.1,\ \varepsilon = 0.02,\ a = 1$, Fox: $n_F = 40$, Rabbit: $n_R = 500$

Here each Part amount is changed by a differential equation that adds all Action fragments affecting the Part.

[1] ODE Model from Otto & Day 2007 'A biologist's guide to ... modeling...' p76 Eq3.18; values: p141 Fig4.17 has a max & min we recompute in 7d; we set 1 TimeUnit=1 Month.

8s **A new stochastic run is unique** and treats each individual Part as **indivisible ➔ Extinction possible!** Populations crash once too much Rabbit feeds too much Fox growth.

Hidden assumptions can affect extinctions in **Ecological Forecast** Time Series

8d **Deterministic runs are identical** assuming each individual Part stays **divisible ➔ Extinction impossible!** Populations will oscillate, pretending Part-mash (¼ Fox...) is alive (!) and keeps populations in perfect balance!

6 **Simulating is testing** *in silico.* For good models, simulations are like experiments in the wet-lab

7 **Storing is deciding** what matters about data and results.

8 **Concluding is learning** how to improve models, data collection, assumptions. Science is done by going back to **1** for the next round ...

7A. Research Statement by Laurence Loewe

My research goals are (1) to predict in detailed simulations how real-world evolution unfolds in cancer cell populations, fruit flies, and other systems (2) improve estimates of the strength of selection by complementing experimental and population genetics inferences with independent Evolutionary Systems Biology (**EvoSysBio**) estimates of Distributions of Mutational Effects (**DMEs**) (3) develop methods to efficiently enable (1) and (2).

Overarching vision: Envision a future where biologists routinely use simulations in a mechanistic framework to predict evolutionary processes for applications such as cancer care. As evolution is governed by selection, predictions largely depend on assumed DMEs and how they impact fitness. Experimental and population genetics inferences that inform current DME overviews reveal critical effects but cannot close some key gaps with evidence-based summaries. EvoSysBio defines how to infer DMEs *in silico* from high-quality molecular systems biology models. Only a small fraction of conceptual models are formalized for simulation, likely due to modeling pipelines with undue complexity (Fig.1). My work focuses on developing a modeling language for biology for accurately describing how parts in systems interact and has a rigorous format for biodata that facilitates uncertainty quantification and parameter estimation. Its design method (Fig.5) safeguards the *language trifecta* of long-term (i) backwards compatibility, (ii) extensibility, and (iii) user-friendliness. This *trifecta* informs all designs from the start, since everything can be added later, except simplicity.

My accomplishments advanced each goal.

1. Predicting mutation accumulation: How DMEs and Muller's ratchet shape an asexual fish genome

For 100,000 years the fish Amazon molly lived without recombining parental genomes, and without its main way to shed harmful DNA changes. These accumulate in a DME-governed process called Muller's ratchet. Its genome was sequenced; I predicted extinction even if rare paternal DNA imports heal some harm [30].

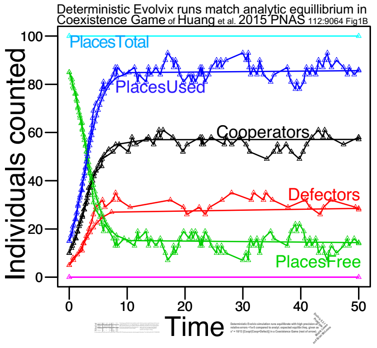
2. EvoSysBio: Completely redefined framework for mechanistic evolutionary systems biology.

My new framework [o2] facilitates defining better maps from genotypes to phenotypes and to fitness by using more types of data and modeling more complex interaction networks. I redefined all concepts; they are now more widely applicable without loss of accuracy; they also have clearer names in preparation for a user-friendly syntax. For example, new names better distinguish correlation from causation. A concise and complete definition for mechanistic EvoSysBio with well-defined fitness landscapes at its core [o2] is a milestone to guide future work. EvoSysBio can now estimate DMEs for more diverse systems and thus better close the gaps in DMEs left by population genetics approaches and experimental observations [o1,o2].

3. Evolvix: a new modeling language to make accurate modeling easier from biochemistry to evolution

I created a prototype for Evolvix, a new modeling language and compiler (available at evolvix.org). It features a user-friendly syntax for formulating models (Fig 1) and querying time series results, automated transformation from a readable model format into the different arcane formats required by the deterministic and stochastic simulators, a graphic user interface and a user's manual. A distinguishing feature is an efficient time series query syntax. It allows users to specify exactly the precision and the results to report, assisting users to trade off storage space vs precision to efficiently collect time-series data from rigorous Continuous-Time Markov Chain simulations of pure mass action formalisms (as in Fig.1, Fig.2). I used Evolvix for all tests of how Lazy Updating can accelerate simulations [26] and many other models in research, teaching and outreach.

Fig.2: Game theory in Evolvix. Changing strategies is how individuals can play formal games in evolving populations. Such games make DMEs dynamic. My group explored a syntax for **Strategy Payoff Tables** that simplifies defining many types of games in Evolvix by delegating the setup of lengthy simulation code to the compiler. Such tables implicitly define related DMEs. Stochastic and deterministic runs shown.



4. Role of divisible vs indivisible individuals for predicting evolutionary processes, and DME estimates

Fig.1+2 show two key simulation approaches: ODEs that treat individuals as divisible and stochastic simulations that assume indivisibility. Simplifying the switch between these in Evolvix allows users to easily explore whether populations in a given model have the size to justify ODEs. The impact of population size on stochasticity is key for many molecular, cellular and ecological models. I built over a dozen models to study stochasticity across domains to find the best designs for such modeling in Evolvix, and lay the groundwork for future publications. For example, my group used game theory to analyze a multi-level simulation model for the evolution of cooperation which does not evolve in deterministic models. Yet, it does evolve in stochastic models that assume indivisible individuals[29]. Such work has a wider EvoSysBio significance: it shows how games can make DMEs depend on population states that lead to dynamic DMEs, which need to be represented in Evolvix (Fig.2).

5. Evolving the Evolvix language by adding programming paradigms and supporting new types of models

The published prototype is a domain-specific modeling language. Its purely declarative style best simplifies implementing key models but is too restrictive for describing all analyses of interest, since it depends on a designer's ability to predict all user needs. Using Evolvix showed me this is impossible, and that users need the power to define new analyses using general-purpose programming paradigms for uncertain biodata. This key insight motivated me to fundamentally change how Evolvix is developed; it now follows the new method for language design (Fig.5) that I defined to enable "*prefactoring*" existing expertise and input from usability experts in order to meet *language trifecta* quality on the long term.

6. FlyClockbase: a prototype Versioned Biological Information Resource (VBIR) for biodata science

Circadian clocks have been studied for decades. My lab is first to report the variance of the daily times at which core clock components reach their maximum (Fig.3). This[F5] is our main result from working with FlyClockbase[b3]. To create this resource, we integrated over 400 molecular time series in the fruit fly *Drosophila melanogaster* wildtype from 86 studies spanning 25 years[b3,F4]. FlyClockbase also establishes a strategy for developing VBIRs[b3] to improve long-term backwards compatibility and portability on many platforms. Such features facilitate use, maintenance and adding data with minimal effort. FlyClockbase assists in hypothesis-driven research as consistently defining and using semantic terms is integral to its biosystem curation as new studies are added[b3]. Biological databases are well known to contain data of mixed quality, yet this observation is rarely quantified. We conducted a quantitative human error analysis while investigating whether potential errors in the data could have affected our main result (Fig.3)[b3, F7]. It will remain important for EvoSysBio to distinguish genuine biological uncertainties from errors by human input or analyses[F13,b3]. For clear distinctions in stored biodata, VBIRs are being designed to support key insights from biodata science[b3].

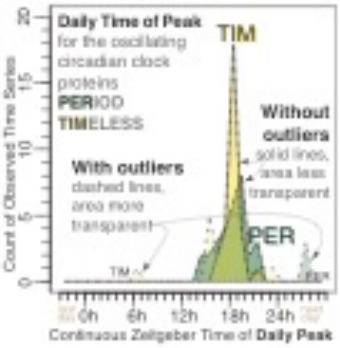


Fig.3: FlyClockbase broke new ground by observing variances that show how different parts of a fly's inner clock hit their daily max with different precisions. Finding drivers of the timing variation can help to understand such clocks better.

7. Quantifying uncertainty: two types of zero in DNA sequence diversity equations nulled DME work

My work[i1] revealed the ambiguous use of zero in common equations for DNA sequence diversity. Zero is used to represent *both,* sites with '*not available*' diversity information and sites '*not applicable*' to the given research question. We found that diversity tended to increase for sites represented less often in raw sequences. This trend is not accounted for in the equations, greatly reducing accuracy of diversity estimates and thus quality of DME estimates[24]. The trend is ignored in the field, but greatly influences inference of DMEs. This type error will be found quickly once Evolvix is extended by general-purpose type checking[b3] and a statistical logic[F08] that can accurately handle biouncertainty[F13].

Future work: towards EvoSysBio predictions of evolution and time series with a powerful modeling language that *remains* stable, extensible, *and* user-friendly

The next steps include finalizing a stabilizing versioning system (see pending grant), expanding Evolvix to read and write VBIRs, reviewing SBML modeling capabilities and solving the respective problems in Evolvix, transforming Evolvix into a Jupiter kernel and linking it into this growing ecosystem for data science, improving its parameter estimation capabilities, and distributed computing. Other tasks like adding programming paradigms and improving a user-friendly interface will be ongoing. Evolvix needs to be developed in conjunction with practical biological modeling to ensure that Evolvix and its tools grow in relevance and usability for solving the broad range of biological questions required for predicting how cancer cell populations evolve in mice and many other EvoSysBio problems.

8A. Teaching Statement by Laurence Loewe

Fig.4 is final, text is refined Refs to be inserted

My main teaching goal is to introduce non-coding students to the modeling skills they never knew they had. I do so I leverage the user-friendly syntax of Evolvix, shared as a free tool, ready for use beyond class, and packed with the same rigorous, state-of-the-art simulation technology I use in my research. In the protected space of class I offer students the chance to spread their wings by modeling a system of their interest and explore real questions with no answers to look up nor a guarantee they even exist. When stuck I use my 20+ years of experience in modeling to assist them in exploring options. Known as problem-based learning, this approach is a particularly effective form of learning and offers students the opportunity to explore aspects of research in biosystem curation that will keep growing in importance. In larger classes I use examples of interest to students to illustrate contributions from modeling, albeit neither hiding potential nor pitfalls of modeling in molecular and evolutionary genetics, EvoSysBio or beyond. I aim to convey importance of quantifying uncertainties in order to be precise and how drawing connections can help to understand individual pieces of the broader puzzles we call biological systems.

> *"A good notation has a subtlety and suggestiveness which at times make it seem almost like a live teacher … and a perfect notation would be a substitute for thought"*. Bertrand Russell, quoted by Woodger 1937 "*The Axiomatic Method in Biology*" p18

Integration with Research and Outreach ***Teaching is a key for research, to students and teachers.***

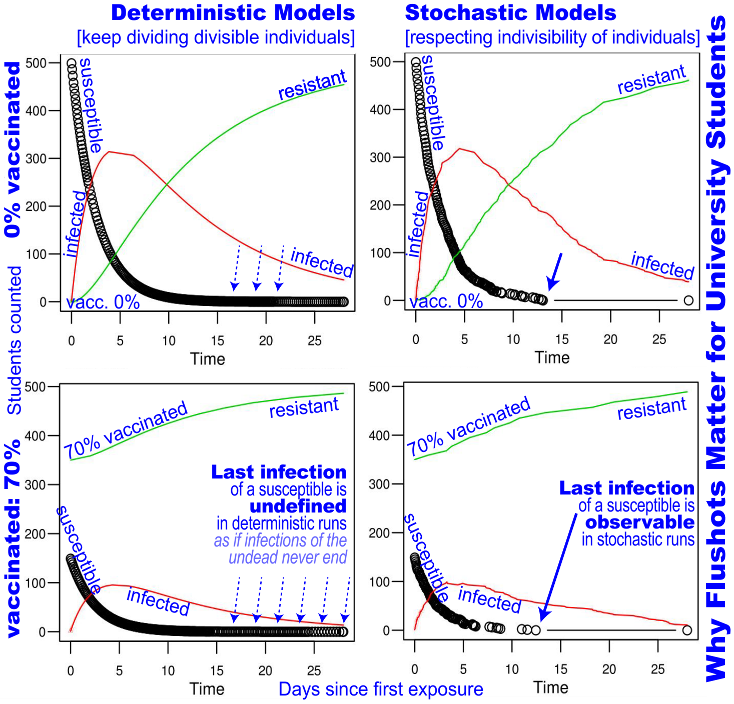
While generally true, this statement has acquired new dimensions since I defined my new method for designing the programming language for biology that I work on (Fig.5). For example, Fig.1 is both product of and preparation for my teaching: while I use it as 'hello world' introduction to Evolvix in teaching, its various aspects keep getting refined as I use them. My work on the architecture and design of the Evolvix modeling language benefits my students by exposing them to a more thorough evaluation of concepts than they might otherwise get, better links to the bigger picture (which I need to define a coherent language), and the practical benefit of learning how to use a tool that simplifies concurrent programming (one of the harder problems in computer science) in order to make it accessible for analyzing the concurrent systems that we in biology identify as biochemistry, ecology, or other.

Therefore, my research can be seen as a preparation for teaching with an emphasis on providing the clearest possible definitions of important concepts and a tool that implements them. Both of these activities could be seen as a preparation for outreach where clarity and usability are tested on more general audiences (which would not be efficient without the hidden ground work of trying to be as clear as I can get without outreach). Yet outreach could also be seen as a preparation for teaching and part of research because issues raised in outreach will also contribute to the overall clarity which benefits teaching.

Goals. Methods. Needs. Vision.

Geneticists have long been at the forefront of integrating biology, mathematics, statistics, and computing. There is a need for expanding training opportunities to offer efficient introductions for geneticists interested in adopting more quantitative computational approaches. I aim to meet that need by using tools that help them to focus on biology and not get mired down with the technicalities of getting code to work. Where possible, I use problem-based learning.

Fig.4: Simulations of flu infections modeled by a student team in my EvoSysBio course. The team made these plots with Evolvix for their final submission, which also biosystem curated the disturbingly low vaccination rates actually found on campuses and official targets, both between the extremes shown here (blue labels are from me and cover some other labels).



Development of new courses: ***Genetics 546*****:** ***Evolutionary Systems Biology Modeling Introduction***

I created this new three credit course with modeling of a wide variety of biological systems at its center. I taught it every year since Fall 2013 and received its official course number recently. This course addresses some deficits in the computational and quantitative skills of students in genetics and other biological fields who are not attracted to more classical math-bio courses. I designed and developed the syllabus for the course as a fellow of the Alpha Cohort of the Madison Teaching and Learning Excellence (MTLE) program. In this course students use modeling to learn how to integrate disparate fragments of information, how to assess their reliability, and how to describe the dynamics of a biological system by creating realistic simulation models that are well understood. At the beginning of the course students choose a research question that they are interested in and throughout the course they work in small teams on building a respective model. The final submission takes the form of a research grant with the presentation of preliminary simulation data and an outline of the next steps in the project including future simulations, values to be measured or curated, possible expansions of the model and the significance of the project. For example, Fig.4 was produced by students in the last course. They would have liked to expand the flu evolution models to more realistic spatial structures, which was not possible in the course. Other projects included so far, the modeling of harmful algal blooms and how they might impact the food chain in Monterey Bay, the potential evolution of the microbiome in human intestines, how heat affects the breakdown of wood as needed for paper production, the growth of a single cancer cell into a population (and its stochasticity), and how Evolvix could be used for game theory. This last project was remarkable in many ways, as it introduced me to game theory, game theory to Evolvix and led Brian McLoone to join my lab as a postdoc for a related project[29]. He is now Assistant Professor at a prestigious research university in Moscow. This problem-based teaching method encourages students to actively integrate their newly acquired quantitative and technical literacy with analysis and creative thinking. The simplicity of the Evolvix syntax and the access it provides to CTMC generated time courses make it easy for students to start modeling early in the course. I test new concepts for Evolvix in the course to sharpen their clarity as I evaluate which aspects work best (compare the new language design method in the Outreach Statement). In addition, the course served to further establish and advance the new field of evolutionary systems biology. Working so closely with students in my research-intensive course, I naturally invited them to become co-authors, when a problem to which they contributed grew into an independent publication (as for example, the other course for which I developed a curriculum to explore basic questions in computational biology; students there contributed much to a now completed study[28]). Getting interdisciplinary courses off the ground is hard, as I learned afterwards. This course meets a steady stream of students that venture from biology to learn more about what modeling might do. I plan to continue to offer and improve this course, which meets an essential need, given how many biology students would struggle to understand the difference between assuming divisibility of individuals or not (see Fig.1). As Evolvix gains features, stability, and more broadly usable programming paradigms and modeling formalisms, I will be happy to explore additional venues for advancing the quantitative and computational literacy of biology students at UW-Madison.

Mentoring of undergraduate students, graduate students, research interns, and postdocs.

I mentored 2 postdocs, 2 graduate student, 6 research interns (who stayed in my lab after graduation), 12 undergraduate researchers, 9 undergraduate paid workers, and 3 project assistants from computer science.

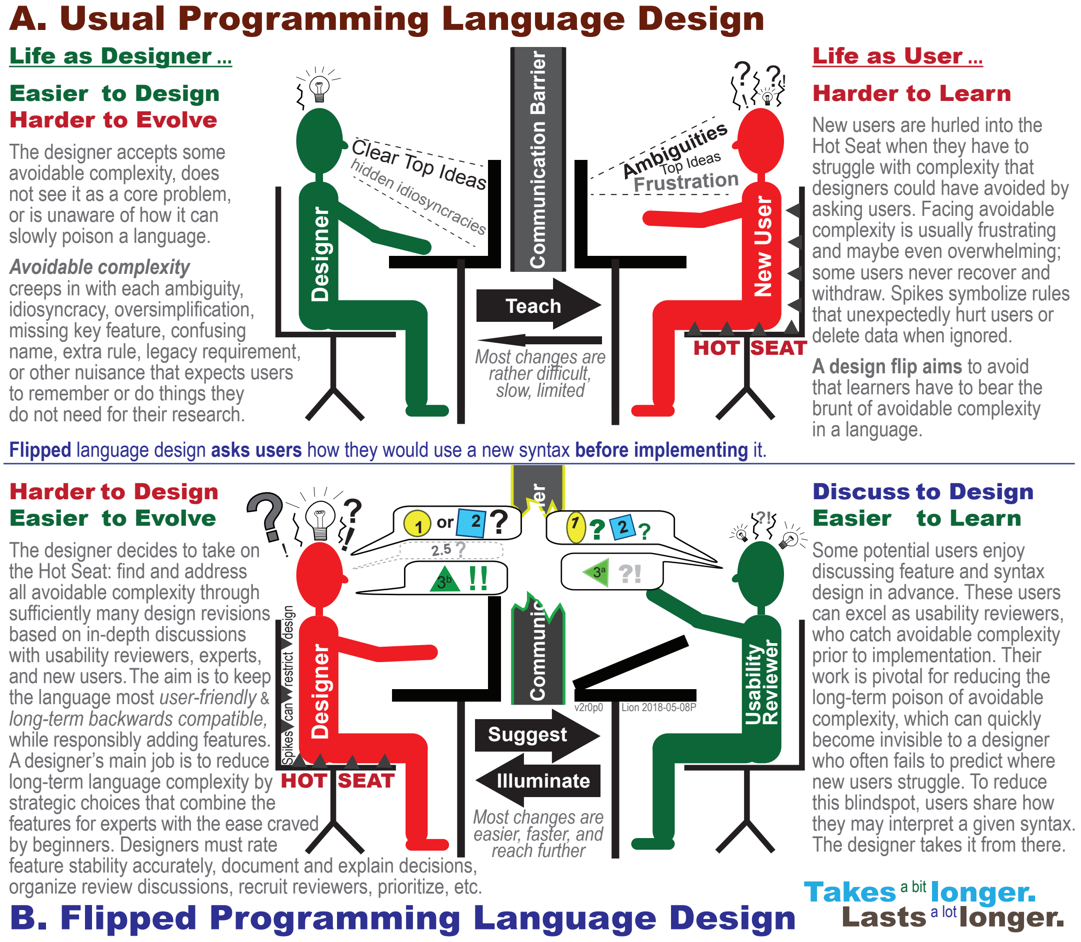
Other classroom teaching and future goals. I taught in the BioCore sequence (population genetics introduction in Semester 1 and an EvoSysBio module in Semester 4). Teaching in larger classes is a great way of testing Evolvix models for broader audiences and I intend to return to that aim at some later point. On the shorter term, I need to address a few technical issues that require my undivided attention in order to offer my students a better user experience. These include extensions of the modeling formalism in Evolvix, as well as integrating it with broader interactive capabilities such as those offered by the JupyterLab platform for data science. I plan to transform Evolvix into a Jupyter Kernel to add the tools needed for an efficient modeling experience to prepare students for the future. The Jupyter platform is one of the up and coming software ecosystems with much momentum in industry and academia and likely to stay. As I build Evolvix for durability, I have to choose wisely in the interest of my students.

9A. Outreach Statement by Laurence Loewe

Fig.5 is final, text is refined Refs to be inserted

EvoSysBio builds simulations on biodata science and tools. Its tools must guide researchers to focus on biology by transparently controlling technical complexity; so, tools must interact well with users, each other, and bio-result representations. My lab is removing rough edges by colliding ideas – not unlike stones in a river – by (i) integrating data, theories, and tools into syntax drafts and (ii) asking diverse users and experts to detect sharp edges by in-depth review from diverse perspectives. Many randomly colliding ideas help me as Evolvix language architect to make its foundations more stable, extensible, and user-friendly. These unusual perspectives inspired ground-breaking insights. Removing sharp edges of theories and tools takes time, which is well spent before users are cut, and the status quo for computing in biology is cemented. To avoid frustrations and improve statistical accuracy in biodata analyses, I developed the *design flip*, an innovative programming language design method that formalizes this long-term user-centric approach I have also been testing in my lab (Fig.5). It reduces how many biologists are immunized against the use of computing tools as a language architect integrates the feedback of diverse usability and expert reviewers. *Skyscrapers dig deep before rising high; thus, for now I do not celebrate 'downloads', but rather 'concepts refined' – and 'all biologists who did not get cut while using immature tools'*. ***Doing otherwise is to ignore basic epidemiology*** *on why immunization works*. Too many biologists waited too long for tool-chains as in Fig.1 that are stable, extensible, and user-friendly in order to assist them in asking better experimental questions by simulating the systems they study. I see it as a scandal of modern biology education that many have given up ~15 yrs after systems biology popularized the key simulation ideas in Fig.1, which are ~40 yrs old. In the frontmatter, I discuss systemic causes for this epic failure of math-bio communication; as expert at these interfaces I see little hope for remedying this tragedy unless new ways are found for integrating biodata science expertise into compilers. Fig.1 was produced by Fig.5 a new method I found and tested, despite many risks and an up-hill battle. I will still take my chances as evidence overall indicates that other approaches are worse. Evolvix in Fig.1 shows the potential (despite being too rough for broad release); biology undergraduates use this prototype in my course to build diverse interesting models (e.g. Fig.4). Exponential adoption across diverse biological fields is trivial to predict – but only once Evolvix can handle all edge cases.

Fig.5: The new Flipped Programming Language Design method developed in my lab. It delays implementation until clarifying how to reasonably satisfy new users and experts with a syntax that meets the criteria required for a long-term stable extensible user-friendly language. Ref Working so closely with users in the design of products is also known from 'participatory design' or 'co-design'.



A. Usual Programming Language Design

Life as Designer ...

Easier to Design
Harder to Evolve

The designer accepts some avoidable complexity, does not see it as a core problem, or is unaware of how it can slowly poison a language.

Avoidable complexity creeps in with each ambiguity, idiosyncracy, oversimplification, missing key feature, confusing name, extra rule, legacy requirement, or other nuisance that expects users to remember or do things they do not need for their research.

Life as User ...

Harder to Learn

New users are hurled into the Hot Seat when they have to struggle with complexity that designers could have avoided by asking users. Facing avoidable complexity is usually frustrating and maybe even overwhelming; some users never recover and withdraw. Spikes symbolize rules that unexpectedly hurt users or delete data when ignored.

A design flip aims to avoid that learners have to bear the brunt of avoidable complexity in a language.

Flipped language design **asks users** how they would use a new syntax **before implementing** it.

Harder to Design
Easier to Evolve

The designer decides to take on the Hot Seat: find and address all avoidable complexity through sufficiently many design revisions based on in-depth discussions with usability reviewers, experts, and new users. The aim is to keep the language most *user-friendly* & *long-term backwards compatible,* while responsibly adding features. A designer's main job is to reduce long-term language complexity by strategic choices that combine the features for experts with the ease craved by beginners. Designers must rate feature stability accurately, document and explain decisions, organize review discussions, recruit reviewers, prioritize, etc.

Discuss to Design
Easier to Learn

Some potential users enjoy discussing feature and syntax design in advance. These users can excel as usability reviewers, who catch avoidable complexity prior to implementation. Their work is pivotal for reducing the long-term poison of avoidable complexity, which can quickly become invisible to a designer who often fails to predict where new users struggle. To reduce this blindspot, users share how they may interpret a given syntax. The designer takes it from there.

B. Flipped Programming Language Design

Takes a bit longer.
Lasts a lot longer.

Letter to Jo New

Overview. Based on the input from the workshop series I have been organizing, [Ref] in 2016 I completely redefined a mechanistic framework for Evolutionary Systems Biology (EvoSysBio), an interdisciplinary research field I helped to create. [Ref] Results were reported in a 22 page chapter chosen as free download to promote 250+ others in an award-winning encyclopedia. [Ref] To advance this vision of computational biology I created Evolvix, a new modeling language aiming to simplify accurate long-term reproducible modeling across biology (Fig.1). I used my NSF Career Award to build a foundation for keeping Evolvix stable extensible and user-friendly. This led me to a new method for designing programming languages that require long-term stability (Fig.5). I tested it extensively. [Ref] To improve the usability of Evolvix, I pioneered two new university courses, complete with new syllabi (Ref), criteria for performance evaluation, and hands-on exercises to facilitate problem-based learning. The innovation in teaching represented by these courses is evident in student contributions to posters at international conferences [Ref] and peer-reviewed publications. [Ref] My EvoSysBio course introduces students to the interdisciplinary research necessary for building simulation models and helps them to start grasping key principles of biodata science, which helps to ground models in biological reality. My other course explored fundamental aspects of computing as needed for enabling an efficient infrastructure for biodata science that shortens onboarding time. I became increasingly aware of the importance of preparing appropriate data structures for helping students to get started with the biosystems curation work that links parameters in models to biological data sets. Much of my FlyClockbase research [Ref] (see research statement) is a response to the need for predefined structures that are ready to use. *Changing best practices in a field takes a long time, as does changing habits*. At conferences I have consistently taken the opportunity to engage audiences using posters and talks to highlight the need for reducing ambiguity and the use of more efficient computational approaches in biology. To refine and complement my outreach strategies, I have been locally engaging audiences of all ages regularly, testing how early children might start modeling [Ref] at the annual Wisconsin Science Festival [Ref] and Darwin Day, [Ref] attracting grant support for the latter. [Ref] I engaged in the local outreach challenge of advocating for my new interdisciplinary modeling course, [Ref] which I learned only later to be a known outreach challenge (see frontmatter). My advocacy for a tighter integration of models and more rigorous simulation approaches contributed to a competitive award for a sponsored 5-day Banff International Research Station (BIRS) workshop, which I co-lead to investigate the mathematics required for EvoSysBio. [Ref] I keep getting invited [2012, 2016, 2018] to write about EvoSysBio; I leverage such invitations for disseminating broader integrative concepts I develop across fields.

Outreach Perspectives. Translating expertise between diverse communities has been at the core of EvoSysBio and Evolvix development for some time. I will continue key discussions in several spaces:

Scholarship and service to advance EvoSysBio. I will build on my latest EvoSysBio framework definition for advancing the cutting edge via meetings (EvoSysBio.org/meetings), teaching, and writing (e.g., a chapter in a 2019 EvoSysBio book I was invited to contribute to). My goal is to improve the science enabling EvoSysBio modeling and to use it for more efficiently navigating mechanistic, dynamic fitness landscapes linked to the real-world data relevant for evolution. This requires tools.

Tool-chains. EvoSysBio is limited by the quality of biological data available for automated processing in a consistent and stable programming language. Hence, I work to build a more stable storage system for biological data that can handle the biouncertainty often found in Versioned Biological Information Resources (VBIRs; see *Research Statement*). This foundational work is best done in collaboration with real-world biology research on a specific VBIR to create *random collisions of ideas* between types of uncertainty in real-world data and often oversimplified data types available. I found this tension to inspire powerful tools and language features for simplifying accurate modeling in Evolvix.

Debug code2brain interfaces. As ideas flow in, their review by *Design Flip* (Fig.5) remains pivotal for keeping the system simple, which is a key for adoption: *Simplicity is highly desirable for a long-term standard.* Languages die when they choke on their own complexity. Engaging users across all ages is necessary for keeping it simple. To keep immature code from frustrating and thus '*immunizing*' users (see above), working in secret with reviewers is ideal – until all breaking changes are done and a solid base can foster exponentially growing adoption, as highly usable and stable software in new niches tends to do.

10A. Service Statement by Laurence Loewe (not yet completed)

- Early contributions to discussions of memory and data storage in WID.
- Set up 'SysBioM' website (still up); it morphed into the efforts that led to the QBio initiative.
- Served on Genetics IT committee; my student Seth Keel and I did much to hire a top IT person.
- Organized EvoSysBio meetings to advance the field (see outreach, cv, and website).
- In 2018 I was almost elected to the University Library Committee (apparently it was a close call).
- Efforts towards simplifying IT through Evolvix language development can be seen as service to the field, but I realize that this does not count, since no official committee has been set up (yet).
- Various other more usual types of service activities such as science fair outreach activities, peer review of papers, peer review of grants, doctoral committee work, etc. (to be compiled and listed).

Proxy evidence for all statements: My CV	See most recent CV with lists of papers, grants, and more (**see attached**). In light of the open questions raised in the following sections B and C, I found it impossible to accurately reflect my work in the usual style recommended in the divisional guidelines without either grossly inflating or trashing my own work – or inventing an entirely different system that would get everybody to scratch their head. Thus, it is probably easiest for everybody if I stick to the classical CV format for now. Upon request I'd be happy to connect 'Refs' in statements to my CV.

Introducing my 4 2 representative publications and 10 biased ways of selecting them

It is not clear, which bias to prefer, when choosing the output that represents my scholarly work (without mis-representing other important parts of it). The papers themselves are provided externally upon request.

The trade-offs are complicated: Depending on which departmental, divisional, formal, intellectual or other criteria I chose for biasing the choice of my "2 representative publications", the winners tend to change and tend to dramatically under-represent other important parts of my work.
Here are the choices I am aware of:

- 3 5 win if selecting for conceptual **importance for future genetics**.
- 1 2 5 7 win if selecting for my contributions to **evolution**.
- 3 4 6 win if selecting for my contributions to **molecular genetics** and systems biology.
- 2 6 win if selecting for my most profound **quantitative** contributions (so far).
- 4 6 win if selecting for **computing** innovations that advance my biology.
- 3 4 6 win if selecting for what my group and I invested **most of our work** into.
- 4 6 win if selecting for useful **algorithms and data structures** I developed.
- 1 7 win if selecting for '*typical genetics my department might like*'.
- 1 7 win if selecting for '*most prestigious journals*'.
- 3 wins if selecting for a book-length documentary on the **challenges faced by biodata scientists who aim to efficiently communicate** across all disciplines it takes to advance biodata science. This 200+ page documentary is being turned into a series of 16 papers.

Thus, readers may pick their selection criteria to focus on papers most relevant to their work.

1. In this paper I quantify Muller's ratchet in the Amazon Molly on the occasion of the reporting of its initial round of genome analyses. I used evolution@home results, which made this analysis efficient. Warren, W. C., R. Garcia-Perez, S. Xu, K. P. Lampert, D. Chalopin, M. Stock, L. Loewe, Y. Lu, L. Kuderna, P. Minx, M. J. Montague, C. Tomlinson, L. W. Hillier, D. N. Murphy, J. Wang, Z. Wang, C. M. Garcia, G. C. W. Thomas, J. N. Volff, F. Farias, B. Aken, R. B. Walter, K. D. Pruitt, T. Marques-Bonet, M. W. Hahn, S. Kneitz, M. Lynch, M. Schartl (**2018**). "**Clonal polymorphism and high heterozygosity in the celibate genome of the Amazon molly.**" *Nature Ecology & Evolution* **2**(4): 669-679.

2. This paper investigates evolutionary game theory models of how likely it is that cooperative behavior survives in infinitely large vs small groups. This made important contributions to the larger question of my lab, which is the study of conditions under which certain qualitatively different results can be obtained when individuals are assumed to be infinitesimally few in infinitely large populations (vs discrete, indivisible, and living in finite populations – as all populations existing in the real world; for a simple example of a similar problem, see Fig.1). McLoone, B., W.-T. L. Fan, A. Pham, R. Smead, L. Loewe (**2018**). "**Stochasticity, Selection, and the Evolution of Cooperation in a Two-Level Moran Model of the Snowdrift Game.**" *Complexity* **2018**(9836150): 1-14. https://doi.org/10.1155/2018/9836150

3. This paper shows why we need biodata science and how this became apparent through the in-depth biosystems curation of circadian clock time-series observations from 25 years of research. This is the first of 16 FlyClockbase reports and contains as supplement the original book-length integrated analysis of the FlyClockbase work produced in my lab.
   Scheuer, K. S., L. Loewe (**2018**). **"FlyClockbase and the emerging panorama of biodata science."** *Database: The Journal of Biological Databases and Curation*
   (nearing submission as FlyC01 in series 'FlyClockbase and the Future of Biodata Science' repacking aspects of initial book-length FlyClockbase study on bioRxiv): https://doi.org/10.1101/099192.

4. This paper presents the design for a system for automated naming support when building integrative models in molecular systems biology and shows how this can help a general-purpose programming language with handling synonyms. It then demonstrates how extending this system to define 'BEST dialects' can simplify naming for very diverse audiences when designing a new general-purpose programming language from scratch (or in the context of many other modeling problems). It concludes by presenting the Flipped Programming Language Design methodology ('Design Flip' in Fig.5), which turned out to be essential for developing the architecture for languages like Evolvix.
   In the list below, underlined authors were associated with my group, *italic authors* contributed as part of contributing to a course I taught, all other authors are diverse independent collaborators.
   Loewe, L., K. S. Scheuer, S. A. Keel, V. Vyas, B. Liblit, B. Hanlon, M. C. Ferris, J. Yin, I. Dutra, A. Pietsch, C. G. Javid, C. L. Moog, J. Meyer, J. Dresel, B. McLoone, *S. Loberger, A. Movaghar, M. Gilchrist-Scott, Y. Sabri, D. Sescleifer, I. Pereda-Zorrilla, A. Zietlow, R. Smith,* S. Pietenpol, J. Goldfinger, S. L. Atzen, E. Freiberg, N. P. Waters, C. Nusbaum, E. Nolan, A. Hotz, R. M. Kliman, A. Mentewab, N. Fregien and M. Loewe (2017).
   "Evolvix BEST Names for semantic reproducibility across code2brain interfaces."
   Annals of the New York Academy of Sciences **1387**(1): 124-144.
   With 74 pages supplemental material at http://dx.doi.org/10.1111/nyas.13192 and updates at http://evolvix.org/naming and http://evolvix.org/post.

5. Writing this paper triggered and then required a complete redefinition of my 2009 EvoSysBio framework in preparation for computational implementation; important conceptual limitations and confusions were removed; many new definitions were introduced, some of which replaced older misleading ones. Milestones for EvoSysBio were defined (including challenges in forecasting cancer evolution in mice and antibiotics resistance evolution in a broader environment). As a result of this work, many complicated name-choices in EvoSysBio were made that greatly simplify the upcoming implementation in Evolvix.
   Loewe, L. (**2016**). **Systems in Evolutionary System Biology**. *Encyclopedia of Evolutionary Biology*. vol 4, pp. 297-318, ed. Richard M. Kliman (chief), Hiroshi Akashi (section). Oxford, Academic Press (Elsevier). http://evolutionarysystemsbiology.org/pdf/Loewe-2016-evosysbio.pdf

6. This paper presents an elegant algorithm for accelerating the simulation of more realistic models in molecular systems biology by showing how to deal with a problem that so far presented a challenge for modeling slowly yet unpredictably changing internal or external conditions. Later it became clear later that this same algorithm provides an elegant solution for how to deal with problems of updating

complex data streams in biodata science as integrated by versioned biological information resources in a concurrent world (many of them form complex networks that are continually updated; see the vision for biodata science developed in the FlyClockbase reports).
Ehlert, K., L. Loewe (**2014**). **"Lazy Updating of hubs can enable more realistic models by speeding up stochastic simulations**." *Journal of Chemical Physics* **141**(20): 204109.

7. This paper identifies patterns in multiple DNA sequence alignments that likely represent signatures of selection. My group did very many in-depth analyses that supports its conclusions; most of them were deemed to be too extensive for this publication.

   It was decided to publish them independently, but analyses were greatly complicated by issues of software engineering that turned out to be prohibitive when attempting to resolve them 'quickly' (without taking the time required for essential strategic planning). Most of these issues could have been resolved with an appropriately constructed compiler made for model analyses with features that are now scheduled for implementation in Evolvix. Thus, completion of this work has been temporarily postponed.

   My group's attempt to obtain the most accurate high-quality dataset for investigating the high-level population genetics questions of this paper, also led to a discovery of profound importance for biodata science, which happens to revolve around problems with how to 'count'. My group found a major new difficulty for calculating high-precision observations of DNA sequence diversity from incomplete next generation sequence data, because it was not clear how to appropriately deal with the two different types of zero that (implicitly) show up in the commonly used equations for computing DNA nucleotide sequence diversity. Understanding the riddles posed by our findings and whether they were caused by problems in our data (no) or were in fact general issues (yes) took a long time to determine. Results now in preparation for submission (same urgency as FlyClockbase reports). A good part of my determination to develop Evolvix is fueled by the astonishing conclusions of this upcoming study, since its core problem could have been detected by an appropriately designed compiler for handling the uncertainties and imperfections regularly seen in biodata science. Without stealing the thunder, it might be summarized by saying: I was good enough at math to be hired as faculty for my quantitatively advanced work in population genetics and modeling without realizing that I struggled to *count* properly (due to my failure to understand what 'zero' really stands for – a problem that turns out to be as difficult as it is common).

   As appropriate for that upcoming paper's topic, nothing about the struggles it reports is found in the following paper, which was written at a time where I was not yet aware of any such difficulties:
   McGaugh, S. E., C. S. Heil, B. Manzano-Winkler, L. Loewe, S. Goldstein, T. L. Himmel, M. A. Noor (**2012**). **"Recombination modulates how selection affects linked sites in Drosophila**."
   PLoS Biology **10**(11): e1001422.

B. Output Diversity example explaining the challenges:

Evolvix Giants of Biodata Science

Illustrates the important recurrent case in my work where a certain important document evolves continually to improve the integration of important interdisciplinary insights. A close look at the details illustrates the challenges of how to 'count' such work in the context of preparing tenure dossiers or other types of progress reports widely used in academia.

Sections:

1. **Motivation for Evolvix Giants**: Why & how to use their list to reduce cognitive overload by memorably grouping related abstract concepts and assisting users with navigation.
2. **Quality Annotations of Evolvix Giants:** how to use key stages of Stabilizing Versioning in Evolvix: why they exist, and how they are used for content for various sections.
3. **My main responsibility as Architect of Evolvix.**
4. **Impact of *Batching Strategies* on progress with implementing Evolvix.**
5. **The actual content of the file 'Evolvix Giants of Biodata Science'**

B1. Motivation for Evolvix Giants: Why develop a list?

How this list can reduce cognitive overload by memorably grouping related abstract concepts and assisting users with navigating a flood of abstract information in various ways.

Evolvix Giants of Biodata Science: a draft introduction and a draft list.
Expecting this summer to work with Jane Jingyu Zhang, the art student in my lab, I spent some time to improve and stabilize the list of giants in order to better cover important disciplines and insights for Evolvix and find for Jane originals from which she can then draw embeddable cartoons for easy long-term reuse throughout Evolvix.

Why?

Ease learning for newcomers. Using *visual, personal, and memorable* details of each giant, I will link key concepts and fields of interest for modeling in Evolvix to those details, in particular their cartoons. Thus, **key abstractions become easier to recognize** in manuals, lesson-plans, error messages, and more. The system aims to assist beginners with navigating an ocean of abstractions that frustrates the modeling ambitions of many biologists. Cartoons of a giant may **smile or frown** to indicate how experts in the area usually assess an idea at hand.

Giants are like 'life-guards' against certain nauseating information overwhelms in modeling.

Length. To remain useful, the list must stay short*ish*; with 42 entries I already push the limits. Thus, the list has to remain idiosyncratic to the key strategies I chose to emphasize for simplifying modeling in Evolvix. This list cannot portray actual history of science (too many giants exist and would make this list useless for newcomers). In order to still cover all important concepts and areas, I have to resort to some anachronisms and pretend each giant has remained active and continued research in the areas I chose for them to represent in Evolvix – sorry to all historians of science; I'll hope to find a way to make amends, maybe by eventually creating more extensive online documents that provide the details.

B2. Quality Annotations of Evolvix Giants: Measuring Progress

How to use key stages of the Stabilizing Versioning System (StabVS) in Evolvix:
why they exist, and how they are used for content for various sections.

Below I describe the quality of the attached Evolvix Giant document using StabVS, which is based on the Evolvix StabilizingZone, followed by implications for reviewing, progress and batching.

Stability of attached pages (measuring quality using StabVS versioning numbers):

- introduction to the list of Evolvix Giants (text and ideas: **QQv1**);
- choice of all persons and their place on the list of Evolvix Giants (identities of persons: **QQv1**);
- refined positions: table overview of giants A-E (**QQv1**);
- raw positions: table overview of rest (**PPv1**);
- full detail example (**PPv1**);

The Evolvix StabilizingZone is used here to mark progress towards long-term stability:

- **QQ = QualityQuest = I invite feedback;** this content is as good as I can make it for now. Please help by reviewing diverse aspects from any relevant angle conceivable.
- **PP = PreProbing = Not yet worthy of reviewer time**, as it is being finalized for review; any contributions are welcome from all who don't mind entering a building site with lots of rough material and aim to assist with making content ready for QQ. Conceptual 'pre-review' criticism is welcome at PP: the sooner fundamental problems can be detected, the easier it is to fix them.

Evolvix QQ review for architectural decisions is much more stringent than scientific peer review, because *all Evolvix users will* have *to accept all restrictions on their Evolvix code that are imposed by all proposals not removed at the QQ review stage or any of the subsequent stages*, namely

RR (ReviewedRelease) or
SS (StableSource).

These stages are meant to prevent the guarding managers of the last stage

TT (TrustedTested)

from prematurely accepting systems, that complicate the work of users unnecessarily over the long term.

B3. My main responsibility as Architect of Evolvix

As Architect of Evolvix I work towards realizing the Evolvix mission. It requires all modelling and programming features to support all three Evolvix hallmarks, namely to make the language

stable,
extensible,
user-friendly,

and to protect these hallmarks **over the long term.**

These non-negotiable requirements are challenging to meet and motivated me to I develop and test the new programming language design methodology described in Fig.5. Accomplishing 2 of the 3 over the long term is a challenge likely to earn respect in computer science or a high-paying job in industry – yet it would kill Evolvix for long-term use in biology. Insisting on all 3 dooms a project to failure if typical modern approaches are used. I know this; that is why I have been developing a new approach. Most programmers and computer scientists with whom I discuss Evolvix realize eventually how big the challenge is – and leave the discussion; they typically do so, before I get a chance to explain why the new approach that I developed gives me a chance to do this nevertheless. Since all 3 are a *must* for keeping biology efficient in general, and EvoSysBio in particular, it is important to try in my analysis. This assumes that biology as a centuries-old discipline still has interesting questions to solve for a century or more. On these timescales almost, all software systems we know today will break.
Yet biology will continue. Without a stable language for describing, storing, and processing biological data, biologists will have to remeasure lost data or manually fix code that is being broken every few years or decades. This treadmill of forced programming language updates is very costly for biology already. This instability is effectively enforced by

- *myriad incentives* that enshrine the
- *need to demonstrate productivity* at all cost in our fast-paced world of computing,
- re-invention and unnecessary complexity are not seen as a problem,
- yet sufficiently thorough review is continually decried as unproductive, even though it is the only productive way out of the treadmill that can save biology from eventually spinning its wheels in the sand.

If my analysis is correct, then the exciting new 2018 NIH data science strategy indicates that NIH has years of costly experiments ahead of them before they realize that much more digging will be necessary to reach a stable foundation.

Eventually, it will become commonplace (I hope), that time spent up-front in reviewing and integrating existing designs is time well-spent, even if “nothing seems to happen”.

When sky-scrapers are built today, the first activity is counter-intuitive: digging a big hole. What is obvious for buildings is not necessarily understood by everybody in computational biology: it is only possible to build as high as it is possible to dig in deep. In the meantime, those who try to avoid reinventing wheels and make some of them reliably work, together will have to fight for every inch of thinking, design, and review time.

The reason why this is to important, is that the exploding costs of changes at later stages (RR, SS, TT), makes it next to impossible to fix mistakes that were unknowingly integrated into the foundations of a complex system. This is particularly true for programming language and compiler design.

Therefore, my main challenge as the architect of Evolvix is to find efficient ways of anticipating the collective wrath, irritation, and contempt that all future Evolvix programmers and users would likely direct towards any particular feature I intend to include into the foundations of Evolvix, making it impossible to change later. I then have to direct this energy of frustration towards any solution I consider to adopt for real. Similarly, with the excitement a feature may bring. After collecting such insights, I need to make a trade-off, determining which programming tasks I will want to make easier in Evolvix, and which ones harder (based on best practices, priorities for the targeted user group, etc.). My goal is to **make it easy for programmers to "do the right thing**" in the interest of scientific accuracy, less bugs, reproducibility, and user-friendliness, while making it harder or impossible to "do the wrong thing".

Therefore, in many ways, QQ review must be as stringent as a review as is possible if indeed overall costs of development are to be minimized.

Since this is a lot of work, I prioritize work on foundational aspects, delaying all non-architectural features as much as possible (after ensuring that Evolvix already supports all aspects necessary for implementing such features later). I developed this new approach despite many obvious risks that programmers tend to point out quickly, *because it is the only hope I see* for producing a programming language for any non-trivial context that stands a chance of reaching a productive lifespan on the order of the designated time of productive use of the Discovery Building (i.e. ~100yrs). Despite appearances, I am not taking uncalculated risks; I have tested the new methodology extensively in my lab at WID, and the most exciting overall result of my research in WID is: *I've found a path to get this implemented!*

B4. Impact of Batching Strategies on progress with implementing Evolvix

I included the Evolvix List of Giants as an example for important integrated interdisciplinary work and the headaches it generates for typical academic performance evaluations. Many important Evolvix development tasks require:

> **integrating peculiar blends of disciplines and activities as illustrated with the attached list of 'Evolvix Giants'** (see motivation above and in the introduction to the list).
>
> **The rigorous review requirements essential for Evolvix create a big problem for reporting progress within many typical management structures for academic and other performance**
>
> For example, compare the most important work for the QQ stage explained above with typical expectations of productivity. This illustrates the core problem, which I identified as a '**difference in batching strategies**' in the main frontmatter text.

After observing myself in many settings and discussing productivity related questions with many others, I no longer think that I still have a problem with lack of productivity (that is *after* medical and other accommodations that took *most* of my tenure clock time to set up). Yet, my new efficiency has only increased the clarity with which I can now identify the root cause:

> **My core research questions require unusual strategies for how tasks *must* be grouped to execute them at speeds that allow for *any* reasonable progress.**

Experiment: The more I organize my research in this new way to accelerate progress on my research agenda, the harder I found it becomes to merely rely on numbers for a fair comparison of my performance with strategies commonly used by my colleagues (making such 'apples to oranges' comparisons fair is currently impossible without relying on additional narrative text).

Counter-experiment: If I reorganize my research *back* to strategies that better match common metrics for performance, then *my research in population genetics appears more productive to my department*; yet my *true progress towards a deeper understanding of population genetics slows down* (as I develop less of the biodata science I need to explore evolutionary systems biology).

This slow-down has likely practical consequences, because it interferes with the main reasons for why I joined WID. I aimed to develop EvoSysBio simulations in Evolvix to the point where they can eventually facilitate a better understanding of how antibiotic resistance evolves and how to fight it.

I have been at the cutting edge of EvoSysBio research since 2007 when I initiated the discussions that led to my definition of the field in 2016. I have observed carefully how innovation, products, and approaches have come and gone. I have observed exciting scientific revolutions and developed a significant intuition for which types of problems are best matched for which types of approaches. I paid particular attention to how innovative software is developed and by whom. Since EvoSysBio is data-intensive I closely observed big data, data science, and a slew of tools and techniques that have been developed and used by the best. These observations have given me a good grasp of opportunities that exist for biology if working links to computational resources can be established.

It makes me sad that most biologists are excluded from these possibilities for reasons that are much more systemic than most enthusiastic supporters of computational biology seem to be able to imagine. I have worked on approaches for reducing this gap and gained pivotal insights into what makes a given approach work – or not.

This has provided me with a panorama of the technological opportunities and *risks faced by any researcher or agency intent on changing the status quo in data intensive computational biology*. There is no shortage of excitement and motivation to get started and to make fast progress on this; the excitement will keep building as biology is about to overtake all other data-intensive sciences sometime soon (see NIH 2018 Data Science Strategy). I have been part of this exciting movement for some time:

- I was as excited when I came to WID in 2010;
- I was as excited when joined the Center for Systems Biology in Edinburgh in 2007 (started by a huge BBSRC grant to bring modelers and experimentalists together to develop a simulation infrastructure and use it for building realistic models);
- I am still as excited about all this as I was – despite all challenges I encountered.

And that is why I am working on Evolvix using the unconventional approach that I use: it's the best chance I can see to get it to work at all by anybody I can think of (assuming they face similar departmental performance requirements). This includes the NIH if it follows the strategy that seemed to have informed their published 2018 Data Science Strategy.

Despite all the excitement for this by so many funders, traditional departments, interdisciplinary research centers, independent research institutes, and more:

I am surprised by my conclusion that there seems to be nobody who can sustain a sufficiently rich diversity of batching strategies to make this work.

Most agencies and scientists seem to struggle a lot to define how research might be measured in this context (without resorting to the more classical measures that are toxic for this approach).

As an example, I attach below the Evolvix Giants document I have been working on over the summer. I plan to publish it with in some form with the FlyC16 paper about diversity in large research projects.

Completing my tenure dossier was much complicated by the question of how to "count" progress on such gradual contributions towards a bigger goal; they are near invisible for traditional metrics, yet matter for my work, because I have many of them.

If you can see a solution beyond "bad luck, throw them away", I'd be interested, if only because I struggle to imagine one.

B5. The actual content of the Evolvix Giants of Biodata Science

The Evolvix Giants of Biodata Science –
illustrating key principles of lasting importance
for those who dare to venture into the unknown

Needless to say, innumerably many researchers have worked hard in order to consistently contribute to astonishingly many disciplines that enable us to day to integrate a relatively thorough view of numerous areas of reality with relative ease (compared to the difficulties they faced in developing the results we can now simply use). Compiling a full list of all contributors is near impossible – as is the task of clearly separating the work they completed form the work that remains to do. Thus, the list must stay incomplete.

The following list of 'Evolvix Giants of Biodata Science' was mostly compiled to break through grey veils of abstraction that can easily obscure important theoretical principles for many experimental researchers in biology. This is not to say all experimentalists ought to learn how to develop theory. This would be an unnecessary distraction from their experiments (except for those aiming to be theoreticians). However, experimentalists can immensely benefit from understanding a few key principles that can help them to appreciate what theoreticians do in order to provide experimental observations in a form that allows theoreticians to make sense of the data. Likewise, the giants here point to principles that also help theoreticians with anticipating important properties of biodata, such as common uncertainties, and the need for automating results analyses in a form that allows future researchers in any area to seamlessly build on these results. This seamless integration is a key goal for the development of the Evolvix modeling and programming language architecture.

The Evolvix Giants of Biodata Science have also been selected to serve the upcoming didactic purpose of marking in the Evolvix manuals the more abstract principles they stand for, along with broader 'catch-all' areas they represent.

By the way they lived their lives, this illustrious group of Giants illustrates another important lesson for biodata science and the evolutionary systems biology that motivated its development: sometimes it takes extraordinary courage and rather unusual career paths in order to develop an intuition for interesting research questions and then pursue them until clear answers emerge. In many cases this required overcoming enormous obstacles by combining a lucid mind with remarkable tenacity. Many of these pioneering giants traveled so far off the beaten path that overcoming the opposition and clichés of their time may seem small to us. However, that would be missing vital lessons! It usually does not take much reading up on their lives to see how daunting their opposition often was and how ruthlessly they were discriminated against, especially many of the early female researchers who worked under the most astonishingly difficult circumstances. Evolvix as a general-purpose programming language designed by biologists for biologists needs to integrate insights from all the giants listed and many more; however, three women played particularly important roles by creating new branches of science that eventually grew into fields that are particularly central to developing Evolvix:

- Lady **Ada** Augusta King, Countess of **Lovelace** (**1815**-12-10 to **1852**-11-27), who laid the foundations of computer science by **showing how thought can in principle be automated** with the help of instructions for mechanical machines.
- Rear Admiral **Grace** Brewster Murray **Hopper** (**1906**-12-09 to **1992**-01-01), who **wrote the first compiler** at a time when others claimed that it was impossible to use English words instead of cryptic code in order to instruct computers.

- Prof. Dr. **Margaret** Belle Oakley **Dayhoff** (**1925**-03-11 to **1983**-02-05), who **pioneered bioinformatics**, which depended on her use of the biological expertise she acquired during her research in order to check the quality of published data and develop the code that helped her to organize and interpret growing amounts of data.

The ground-breaking work of these and the other pioneers below illustrates the disciplinary breadth and depth of expertise and abstractions, required for designing and refining a *stable*, *extensible*, and *user-friendly* software architecture for a compiler that can handle the high levels of uncertainty and complexity often found in biology. All three of these properties are essential. Without useful extensions, who will want to use it? And without stability, who will trust this system with their data? And if data cannot be preserved in consistent, readily accessible ways, then we can no longer contribute to the great biological adventure of compiling a consistent and reliable record of observations for subsequent analyses. As a result, biology will be spinning its wheels in the sand.

The list is long enough as it is and has probably already been pushed to its tolerable limits. To avoid complete confusion for readers in a manual, this list had to stay somewhat short. Thus, it was deliberate to nearly make no attempts to cover all important disciplines, fields, key concepts, or pivotal researchers and their respective identities. Use for navigation in a manual also requires quick identification. This will be done by associating visually using cartoons; textually using nicknames for persons, their core principles, and broader areas; and for maximal brevity, each giant also gets a dedicated symbol in the Evolvix manual using:

- 26 upper-case letters (semi-mnemonic reminders, either of the Last or First Name of that person, or of a key concept represented; adding lower-case letters or many more special symbols would make it much more unwieldy; instead),
- 10 digits were added, and
- 6 frequently used symbols that may also be used in filenames or paths.

To keep the list more engaging, memorable, and diverse, many well-known scientists with more typical lives were omitted on purpose. Given the intended human use for the names in this list, it was attempted to find the most natural fit possible given the various constraints. For example, researchers were assigned to letters that either started their last or first name to match the English alphabet; this worked well with few exceptions. Other mnemonic bridges were constructed where possible to minimize arbitrariness.

Hopefully, this list of giants can help some readers to bring some important abstractions to life that are otherwise easily lost in the wealth of information contained in technical manuals. The choices of giants, their key areas, core emphases, cartoon pictures, and reasons for highlighting them here in this way are almost as idiosyncratic as the lives lived by these giants and the approaches they found for developing their science.

Different entries in this list might also get used as follows:

- Cartoon icons for illustrating the manual for the Evolvix compiler and associated explanations of modeling.
- Names can serve as local ad-hoc network IDs when needed in study groups or classes spontaneously assembled.
- Names can serve as ad-hoc role names in descriptions of different roles in ad-hoc collaborations, where each role is assigned to a pre-defined list of jobs (in order to accelerate setup).

Evolvix Giant Info Record Fields that store details as needed

1. **Evolvix Nickname**
   a. **Explicit** (most frequently used form of the nickname): **Ada**
   b. **Brief** (ASCII character symbol, conditional on a context requiring a nickname): **A**
   c. **Position** (ordinal of this Nickname's position in this sequence of Nicknames): **1**
   d. **Technical** (combines a giant's best-known English name with their core principle): **Ada_Lovelace_Automation**

   These Nicknames are destined to be included in the language core of Evolvix eventually, even if all other biographical details are not to keep the overall size down. Their intended use is to serve as small, reusable, semi-memorable names that can be readily used for various local functional roles that would otherwise require making up a set of labels that (from experience) often result in awkward names, requiring further explanations which are unnecessary if these names are readily recognized as part of a re-usable local set of labels that is made for easy reuse. Such ad-hoc definitions of roles in Evolvix include:

   e. **Host names** for computers of participants in purely local networks (e.g. get devices of locals to interact in class-rooms, workshops, or other ad-hoc meetings using WLAN, WIFI, Bluetooth, or other technologies; idea inspired by a UC San Diego Super Computing Center class room)
   f. **Role descriptions in complex tasks that require collaboration** can use these nicknames for naming the respective agents that act in these roles. It is then understood in the context of Evolvix that these nicknames have to be replaced by real persons (or their computers) when the whole recipe is used in a real-world scenario. Computer scientists have long used 'Alice' and 'Bob' to simplify discussions of communication between two parties; think of the nicknames provided here as an extended scheme for describing many more such roles in cases where no clear functional role name can be defined in a meaningful way.

Need more than 42 Nicknames? Then the list can be extended by appending running numbers at their end. How exactly these are assigned is detailed elsewhere to make sure that edge-cases are handled correctly (e.g. '_0' indicates undefined, '_1' refers to the default name without any running number suffix and '_2' is the first real running number extension; it may be required that '_2' be appended to each giant, before '_3' can be appended anywhere). Adding more giants is not anticipated in this context and would defeat the purpose of having such a centrally defined list. It is of course possible to create many other similar lists that are longer or shorter by using Evolvix language constructs; they will just not be built-in, ready for use, batteries included.

Principles for defining this list of Nicknames (except for the Brief Symbols): Explicit Nicknames must be written in core English to be usable in core Evolvix (i.e. without Unicode). They must be brief and memorable, without spaces or underscores. Explicit Nicknames seek a match between the respective brief symbol letter and (i) the first letter of the surname, or if impossible, (ii) the first letter of the given name, or if impossible, (iii) the concept this giant stands for. Here 'impossible' refers to assigning a name to each letter in the alphabet to make the overall system easier to use. After assigning a giant to each letter, the 10 digits are used for giants with more mathematical or quantitative interests and special punctuation symbols for giants who stand for abstract concepts in Evolvix (vaguely linked to a symbol's shape where possible). These principles are for designers not users; they were used to select the Nicknames listed below.

2. **Evolvix Concept Representation**

   a. **Named Area Catch-All Extended**

   b. **Explained Area** (InfoBlock)
   This is a catch-all for Evolvix specific extensions of some specific area(s) investigated by these giants within the discipline they worked in; catch-all means they represent everything in this area except if more specific sub-areas are represented by some other giant(s).
   Usability, anachronisms, complexity, and the history of science. The Evolvix specific extensions of these topics are used to reduce the complexity of the list of giants and the areas they represent. The lists are idiosyncratic to the biodata science as implemented by Evolvix and neither is meant to be a historic account of who exactly made which important discovery at what time. Hence, the list is not free from some anachronisms, as occasionally newer developments are represented here by older giants who worked in the respective area. Technically, they could not have known about the more recent work; yet, they likely would have if they had lived longer and had continued to work at the cutting edge of their discipline.
   For example, Emmy Noether was a pioneer in abstract algebra. She died before category theory was defined, let alone before it gained traction later in the 20th century; she would most likely have taken great interest in such work and thus might have contributed, since it can be seen as an extension of her work, which identified ever more general (abstract) principles in the algebraic structures she investigated.

   c. **Named Principle**

   d. **Explained Core Principle** (InfoBlock)
   A specific principle of particular importance for modeling or computing with Evolvix that was found by this giant or that is well illustrated by something they did as part of their research.

3. **Biography**. *These and all other following fields will remain open for quite some time and possibly forever.* Some historical details are trivial to establish, others require scholarly work, and some remain hidden in a shroud of mystery that can only be lifted by yet unknown authentic sources that may not exist or never be found. Hence, the stability of the respective information cannot advance beyond StableSource in principle on the Evolvix StabilityScale. This does not make it impossible to include the Evolvix Giant Nickname List into long-term stable variants of Evolvix; the list can be fixed by social contract, even if some aspects of these giants' lives remain shrouded in mystery. It does not take long to recognize that some aspects of every person's life – no matter how recent or how well-documented – will always remain shrouded in mystery.
   Thus, only the briefest initial sketches are given here; they are intended to act as seeds that grow and mature as more relevant details are being added and their presentation is improved.

   a. **Family names**
   in English spelling like the First names; start with most recent name, separate by comma, indicate time period during which the name was relevant in parentheses after the name (e.g. Lovelace, King (1835-1838), Byron).

   b. **First names** and Middle Names
   as written in English following each giant's preferences if possible while only using English alphabet
   c. **Titles**
   starting with typical summary used towards end of life if the list is long (use core English alphabet)
   d. **Synonyms of Full Name**
   list in all relevant languages, using Unicode where needed; start with the equivalent of the Technical variant of the Nickname; give combinations with titles if non-English variants exist.

   e. **Born** (Date / year / range of years) in (Place: city / country / ancient empire / etc. as known) to (Parents info)
   f. **Died** (Date / year / range of years) in (Place: city / country / etc. if known) from (cause if known)

   g. **Brief Biosketch Overview**
   InfoBlock with a very brief biographical overview of key events in the life of this giant. Cite refs with more details

   h. **Research areas (general)**
   Brief sketch of areas they worked in as generally recognized (independent from Evolvix).
   i. **Research results (general best known)**
   Brief sketch of their most important findings as generally recognized (independent from Evolvix).

4. **Challenges.** Some of these researchers had to overcome remarkable challenges to do their work. Note memorable instances in the generic introductory field if they do not fit one of the more specific challenge categories below:
   a. **Educational** challenges: how did they get started with their research?
   b. **Employment** challenges: how did they stay in research?
   c. **Funding** challenges: how did they pay for their research?
   d. **Truth2Power** challenges: instances where they courageously defended their convictions in face of adversity.
   e. **Imperfections Known.**
   We are all children of our time and even as adults remain remarkably blinded by what might be called 'zeitgeist'; another way to put this is that bubbles are hard to detect by those caught up in them until they burst. The giants in this list are no exception. Sometimes their blind spots are easy to see with the benefit of hindsight, but often it is less clear what they did or did not see and why they may have acted in the way they did. Regardless of the details, potential or real short-comings do not invalidate their contributions. This InfoBlock comments on known or debated blind spots, dark corners, idiosyncratic zeitgeist imports, or other conditions, which illustrate that imperfect researchers can still make important contributions, and likewise, someone who makes important contributions in one area is not necessarily free from the many forms in which errors can occur in other areas.

Overview of all 42 Entries of the Evolvix Giant List

Next steps ToDo:

- Text above and entries A-E below have been edited to level QQv1
- All entries after F need to be brought up to speed (currently at PPv1).
- additional Record Fields and InfoBlocks are to be compiled after this table

Brief	**Explicit Nickname In Evolvix**	**Given Names**	**Surnames**	**Challenges faced**	Why chosen as Evolvix Giant?	**Extended Area represented in Evolvix**	**Core Idea represented in Evolvix**
A	Ada	Ada Augusta	Lovelace, Countess of Lovelace, King, Byron	Work outside of academia as ‘lady scientist’; navigate poetry-math tension	First saw the far-reaching opportunities of programming	Computer Science	Automate thought
B	Barbara	Barbara	McClintoc	Faced strong discrimination; despite lack of math training, she correctly challenged a calculation by Sewall Wright (a biomath leader).	Opened the quest for rules organizing any type of complex sequence. Won Nobel Prize for showing how transposons modify genome sequences	Limiting chaotic sequence organization	Irregular changes to combinatoric outcomes add diversity
C	Curie	Maria S.	Curie	Faced strong discrimination, lack of funding while doing her key work.	Worked towards standardization despite winning 2 Nobel Prizes in 2 categories (is still unique!)	Standardization in all areas	Standards simplify communication
D	Darwin	Charles	Darwin	Worked outside of academia as ‘gentleman scientist’; faced much opposition as his work was disliked by major institutions.	Integrated incredibly many details to distill the evolutionary mechanism as abstraction.	Evolutionary Biology, Evolutionary Mechanisms	Many small changes can accumulate in populations over time
E	Emmy	Emmy	Noether	Faced strong discrimination, worked for many years without official funding	Showed how even structures in algebra can be simplified by further ongoing abstraction	Mathematical Abstractions	Abstract to uncover more general patterns
F	Franklin	Rosalind	Franklin				Spatial Structures
G	Gilbreth	Lillian Moller	Gilbreth	Spacetime org-obs efficiencies.	Make work human - OK	Engineering +Org+Psych	Ergonomics user-friendly + efficient
H	Hopper	Grace	Hopper				Automated translation of well-designed code2brain interface
I	Isaac	Isaac	Newton	Invented calculus etc		Infinitesimalization	Modeling: mechanistic + simplify
J	Johnston	Katherine	Johnston	NASA: “Girl Computers” are beating the engineers			Simulations and numeric accuracy
K	Kurt	Gödel					Incomplete+Logic
L	Lamarr	Hedy	Lamarr	Actor + Inventor	communications	Elegant communicate	Security communicate et al.
M	Mead	Margaret	Mead		Cross cultural anthropology	Identify and translate common themes	Designs that communicate well and respect each culture.

N	Nightingale	Florence			Stats descript		BioDS + descriptive stats…+VBIRs?
O	Ostrom	Elenor	Ostrom	Evol Bio, Game theory? Economics?		Values matter and can be shaped by negotiation	Commons Care
P	Peter	Rozsa	Peter		Functional MO,	Logic?	Recursion…+ context changes
Q	Queer	Haldane	JBS			PopGen easy	Paradoxes…
R	Rosalyn	Rosalyn Sussman	Yalow	1921 – 2011 1 in 400 engineers	Medical Physicist	High-Tech Medicine	Tracer concept (use in simulations too…)
S	Sophie	Sophie	Germain	Number systems + Applied Math		PDEs, Boundary conditions	Frequencies, Elasticity.
T	Turing	Alan	Turing		Computing, Dev Bio	Modes of computing	MOs, Finite State automata, Halting problem
U	Uncertainty	Thomas	Bayes				
V	Vasili	Vasili	Arkhipov	Cuba Crisis: he had 1 in 3 vetos and used it to stop nuclear war!	Application of Logic for decisions	Rational decisions despite lack of data	Correctly handling absence of data in extreme pressure
W	Wu	Chien-Shiung	Wu	1912-1997, should have received 1957 physics nobel-price	Nuclear Physicist		Reality ruining a nice theory
X	Xray	Dorothy	Crowfoot Hodgkin	Xray crystallography		Inverse Problems and parameter estimation	Xray the Obs to infer models of the reality that generated the Obs.
Y	Yonah	Ada. E.	Yonah		Ribosome	Encoding? MAA + ThD??	Structure-function relationships
Z	Zero	Albert	Einstein	Get theory right in the last minute after decades of thinking about zero	Spacetime Energy-Matter	Relativity in all places	Zero is relative and the world can be explored in 'thought experiments'

Brief	**Explicit Nickname In Evolvix**	**Given Names**	**Surnames**	**Challenges faced**	Why chosen as Evolvix Giant?	**Extended Area** represented in Evolvix	**Core Idea** represented in Evolvix
0	Algoritmi	Muhammad ibn Musa	Al-Khwarizmi (formerly latinized as Algoritmi)	Indian-Arabic Number system Get Zero, decimal numbers into Europe and define algebra	rejoin and balance Reduction balancing, completion, rejoining	First Steps in Math (800 – 1600, Isaac)	elementary number system, arithmetic, and algebra
1	Ramanujan	Srinivasa	Ramanujan			Indivisibility of individuals	Respect for integers
2	Mendel	Gregor	Mendel				Combinatorial explosions of possibilities
3	Dayhoff	Margaret	Dayhoff	Born 1925	Initiator of Bioinformatics	Bioinformatics MAA, ThD	Alignments, Thermodynamics
4	Ohta	Tomoko	Ohta	B1933	PopGen Hard OR multi-locus or Sampling vs ..	Sample vs infinitesi imalize…	SDMs many small effects can work together
5	Charlesworth	Deborah and Brian	Charlesworth	PhD 1969, b 1943	Multi-locus pop-gen and more	Integrate it all on Evol	Balancing, Bg, sweep Selection rec … 5 forces

6	Leonardo	Leonardo	da Vinci		STEM+Arts + Humanities	Overall integration and design catchall	Engineering design and general catch-all
7	Euler	Leonhard	Euler				Beauty in Maths
8	Paul	Paul	Erdös				Networks
9	Heisenberg	Werner	Heisenberg			QED+ electro magnetism + wave particle dualism	Fundamental limits to knowledge
Brief	**Explicit Nickname In Evolvix**	**Given Names**	**Surnames**	**Challenges faced**	Why chosen as Evolvix Giant?	**Extended Area represented in Evolvix**	**Core Idea represented in Evolvix**
-	Cannon	Annie Jump	Cannon	Astronomy			Eye-balling to link theory and data
.	Occam	William of	Occam	Free Speech, Responsible speech (press as responsible vs ? vs platform as irresponsible)			
/	Linne	Carolus	Linnaeus				Systems for naming and recognizing observation types
+	Trachtenberg	Jakow	Trachtenberg		Developed mental arithmetic while prisoner in a concentration camp		Arithmetic and numeric precision
*****	Cotterman	Charles	Cotterman				Linking genetics to abstract mathematics

Next steps for the Evolvix Giants file:

Todo: **Transform all 42 Entries** in the table above into a more flexible Evolvix Giant List of their Record Fields and InfoBlocks for adding content beyond what fits into the table above.

(I) Overview of the all potentially relevant Record Fields and InfoBlocks:

1. Evolvix Nickname: a. Explicit b. Brief c. Position Number d. Technical
2. Concepts: a. Named Area Catch-All Extended b. Explained c. Named Principle d. Explained Core
3. Biography Personal Names: a. Last b. First names and Middle Names c. Synonyms of Full Name;
Life Context: d. Born (when) in (where) to (whom) e. Died (when) in (where) from (why)
f. Biosketch g. Research areas (general) h. Research results (general best known)
4. Challenges: a. Educational b. Employment c.Funding d.Truth2Power e. Imperfections
5. References

(II) Example Entry

(ToDo: find better formatting)

A (Symbol) **1** (Pos) **Ada** (Nickname) **Ada_Lovelace_AutomateThought** (Tech.Name)
Computer Science (2a Area) Automate Thought (2c Principle)
Biography: Names: Lovelace, King (1835-1838), Byron (3a) Ada, Augusta (3b First)
Countess of Lovelace, Lady (3c Titles)
Synonyms:
Context: Born 1815-12-10 in London (England) to a highly educated and religious mother bent on using math to 'cure' poetic traits from her father, a poet who left a month after the birth. Died 1852-11-27 in London (England) from cancer at age 36.
Biosketch: Ada kept an interest in math and poetry throughout her education and life. Collaborating with Charles Babbage, she wrote the first computer program for his Analytical Engine and realized the broader potential for general-purpose programming of questions that much exceed the mere manipulation of numbers, once appropriately encoded.
Area: Computer Science, Programming
Results: Wrote the first program on paper, conceptually to be translated into punch cards;
First made the conceptual leap to general purpose computing by realizing that arbitrary functions could be encoded, representing arbitrary manipulations of arbitrary data.
Challenges: General: No formal institutional affiliation, no computational thought had occurred anywhere yet. Died age 36 from cancer. Never knew her father. Struggled with her mother's attempts to 'cure' the 'insanities' she may have received from her father.
Education: Various: mathematical and other education.
Employed: No formal employment in science.
Funding: 'Independent Lady Science'
Truth2Power: As daughter of the poet Byron pushing boundaries may have been part of her identity. At a time where many thought that algebra was one of the highest forms of human thought, Ada laid the foundations of computer science by showing how it could be automated in principle with the help of mechanical machines and could be used to automate general sequences of data manipulations.
Imperfect: TBD

References:
Lovelace (1842) "Notes on Sketch of the Analytical Engine …" http://www.fourmilab.ch/babbage/sketch.html
http://jeffreykegler.github.io/Ocean-of-Awareness-blog/individual/2013/07/lovelace.html
https://en.wikipedia.org/wiki/Ada_Lovelace

ToDo: Find better references, better summary texts. Incorporate

C. Other Output Diversity examples: some recent WID Symposium Posters and more

This material illustrates another important recurrent case in my work. Here important results are integrated on posters. Some of these go on to be published as papers and some do not. Either way, these types of posters capture summaries or overviews or details that make valuable points in a useful format, irrespective of whether they are published eventually. Not all of these posters have been formally 'presented' at a meeting, yet all of them have been used in some discussions.

These examples further illustrate the challenges of how to 'count' diverse work in the context of preparing tenure dossiers or other types of progress reports widely used in academia.

Content

1. **Poster: Ecological Forecasts** of Fox and Rabbit with Evolvix (larger than Fig.1 above)
2. **Poster: Interdisciplinarity** of my work as explained
3. **Poster: Why Biology needs its own language** for general-purpose programming
4. **Evolvix**: How to efficiently record time series.
5. **FlyClockbase**: Are VBIRs like FlyClockbase the new genome projects?
6. **Poster: My lab in WID** as described for the WID symposium
7. **Giraffe: different roles** in the scientific enterprise
   and potential steps towards implementation.
8. **Interdisciplinary Whiteboard Discussion Starter** exploring whitespace in-between disciplines by accident (I developed and tested it in evosysbio-course.discovery.wisc.edu).

Interdisciplinary Whiteboard Discussion Starter

exploring **Whitespace In-between Disciplines** accidentally

Laurence ‘Lion’ Loewe

Prepared for and tested in the http://EvoSysBio-course.discovery.wisc.edu/ (Genetics 546, developed at WID), 2016-10-27 (v1r0p0); updated: 2018-10-04 (v1r0p1)

Need: Big whiteboards with many markers (or blackboards with chalk, flipcharts, GoogleDocs, or the like) *and space for all participants to simultaneously write* on a part of the whiteboard everybody can see.

1. **All at whiteboard**: *Note your area of expertise* in about 1-3 keywords (ca. 2min)

2. **All at whiteboard**: *Change perspectives by moving* into a new area (<1 min)
   a. that is *not* your area (i.e. you know very little about it) and
   b. that *might be interesting* to *someone* with your background (*not necessarily you*!) irrespective of whether you yourself find this interesting (*no need to ‘own’ questions*!)

3. **All at whiteboard**: *Simultaneously, silently ask 1-3 easy questions* in writing (ca. 5min)
   a. choose *a simple beginner’s question* in the area you moved to and write it down there:
      i. *if you think someone* working in the area ought to be able to answer it;
      ii. *irrespective* of whether you found ‘a good question’ (this is not important);
      iii. *avoid* ‘*clever*’ questions that do not worry beginners (answers get hard to follow).

4. **Get expert answers:** *Go in sequence or roll dice* to pick experts without replacement (rest time)
   a. Get *each expert to answer one question* before answering another one. Experts have to try to:
      i. *answer* in a few sentences, max 180 sec talking time (use a big fun alarm as ‘Stop’!);
      ii. *allow* 1 follow-up *question* from a *beginner*;
      iii. *allow* 1 follow-up *expert answer* to the *follow-up question* (shorter *is* better)
   b. Take turns until the *experts* in the room have answered all questions from beginners or time runs out…

Modifications are easy and can increase fun, flexibility, feedback, and functionality on the way to starting lively interdisciplinary discussions between experts who might not otherwise connect.

- Allow *beginners* to add questions to the whiteboard at a later stage (2nd round; continually; etc.)
- Allow *experts* to take a brief moment to prioritize the questions received to maximize some goal
- Keep a *record* of all questions and answers, whether as audio/video, or as text does not matter
- If *new questions keep* arriving, erase older ones, and penalize the repeating of older questions
- Set up a jury for the best, funniest, most daring, … question or answer seen in a discussion
- Test out, *how long* certain combinations of disciplines can productively engage without tiering
- *You name it*: extra points for discoverers of different names for identical ideas in different disciplines. Naming is hard, historic, and idiosyncratic. Why not have fun cracking the code?

Ultimately, keep asking ‘**Why?**’ and ‘**How?**’ :- You will cross paths in many disciplines eventually.