

EvoSysBio, Evolvix, and World War V against Coronaviruses: Why reasonable, *wid-e* research is key to victory

Laurence Loewe¹ and the Evolvix Thinkers²

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SO: Main Text Figures

Supporting Info in separate file

Abstract

When a researcher dies, a library burns. This adapted African proverb illustrates the tragic loss of valuable insight. It increasingly applies to websites, and even to our own memory as we get overwhelmed by floods of more data than we can use. The cost is steep: we often know more than we believe as we struggle to integrate our insights. Dividing the complexity by disciplines with simplifying assumptions removes our need to view most complexity of the elephant in the room: a real-world biology often refusing to simplify. Biology has long been *the* discipline of complexity, diversity, and exceptions. Despite its data explosion, biology remains steeped in all sorts of uncertainty we must handle or risk our ability to understand biological reality. This matters for evolutionary systems biology (EvoSysBio), as many challenges of our time require more integrated analyses than ever. These questions have been growing over years of work on Evolvix, a language aiming to simplify modeling for EvoSysBio. Analyzing use of an Evolvix prototype shows why it has to become a general-purpose computer language for all biology if it is to serve the EvoSysBio needs for a reliable statistical logic of biuncertainty and data-integration. Designing it well requires breaking new ground and approaches that build on wide interdisciplinary *diversity-encouraging (wid-e)* research. New at first, *wid-e* research turns out to be widely used for complex real-world problems, albeit with less support than it deserves. These lines of enquiry all cumulate here.

EvoSysBio and biodata science that inform work on Evolvix are used here to model the pandemic of COVID-19 in the US (~3 million infections). Modeling shows (i) simple pandemic timers can predict the brunt of this slow-motion explosion of coronaviruses and when life can go back to normal again, even if many biological details are ignored. (ii) A more complex SIR-style model (termed ‘PandemicSociety101’) can simulate diverse types of death rates and thus help to understand the astonishing variability seen around the world. (iii) Offering a simplified testing-lab model it shows how easily a mirage termed ‘linear fooling’ can subvert a key purpose of testing. (iv) Many SIR models transmit all viruses except for those in ‘removed’ individuals; the model used here forces virus *Shed* and *Catch*-Actions, with a possibility for *Decay* before infection. This thoroughly changes the dynamics: herd immunity offers next to no protection for the doubling times observed in the US without interventions. Yet, surprisingly it might also not be needed: results show how a few-fold change of viral *Shed*, *Decay*, and *Catch* rates can stop a >289+ million pandemic that starts at 1.5 million infections at <5

¹ Middleton, **WisdomConscienceIntegrity**, 53562, United States

email: Loewe@evolvix.org ² see comment in Acknowledgements Section

million with neither herd immunity nor vaccines. However, the need to wisely steward infection risks vs costs to avoid larger infrastructural damages across society requires a surprisingly large amount of microbiology, modeling, and other research that must address many questions at the fringes of several disciplines. The results of such complex research also have to be communicated efficiently to those who need them most: the groups with the highest infection risks. While these requirements pose substantial challenges for current approaches to organize research, these approaches are not set in stone. A careful analysis shows that they are not only worth changing in light of a pandemic, but also for many other reasons, not least to drive a new culture of innovation that might even revive the Rust Belt with research. Yet, how might that occur?

This study presents a work-logic cascade that can in principle choke off the current Coronavirus slow-motion explosion. It leverages the idea of offering a perspective for *wid-e* research that equips all who want from the general public with the tools required for convincing themselves of how to think of the virus in light of the available evidence – without the need for either fear or defiance. In big and diverse countries likely every subculture needs their own boot-camp style for learning best; from book-clubs to gamifying: the broader the appeal, the better. To realize the small chance of still stopping the worst of this pandemic certainly requires an army of volunteers who throw themselves into the task (an army of supporters who enable their work). The required research, data-organization, and training needs are vast; fighting this pandemic has been termed World War V against viruses before. Yet, WWV is only a useful analogy if the highly unusual nature of this war is clearly understood: the highest goal is to collectively grasp the truth about these tiny invisible particles we call viruses and act accordingly. Integrating the work-logic cascade developed here with the simulations given, a strategy for WWV is presented that also includes some ground-rules for keeping WWV as safe as possible for everybody. For example, it is easy to show why people can only join voluntarily and a new approach for coordinating information flow more efficiently is key to prevent costly splintering of key data (the solution proposed leverages Evolvix work towards developing so-called ‘ReRafts’ which are being designed at ReRafts.org to become life-rafts for saving insights from sinking to oblivion in floods of data). This splintering is another ongoing slow-motion explosion that must be defused to win; without the best strategies we can get, we jeopardize our chances for victory. As in all wars, logistics is key for WWV; hence, everybody *can* contribute *something* if they choose to and become a front-line worker (like nurses or doctors, just at another front): writing jokes (as in Taiwan), making face-masks stylish, inventing virus-safe greeting styles, and myriad other tasks can be as important (see work-logic cascade). Is WWV a waste if SARS-Cov-2 ‘simply disappears’? No. It is key to stop the next pandemic at a death-toll avoiding the few Hiroshima bombs this one already took – and *wid-e* research starts a formidable engine of innovation mostly overlooked so far. The US fought for four freedoms in WWII that are necessary for winning WWV now; however, to win in WWV everybody who is interested also needs to be given a 5th freedom: the freedom of research. This study shows how by building on [Nuffieldbioethics.org/publications/research-in-global-health-emergencies](https://nuffieldbioethics.org/publications/research-in-global-health-emergencies).

This file has all Figures with captions sorted into the structure of the study.

Overview of Sections. After the introduction, **Section 2** introduces key modeling basics and the importance of *wid-e* research, which will be referred to throughout this study; given how many widespread misunderstandings of modeling critically hamper fighting the pandemic, this is time well spent. Here we will also briefly introduce the Evolvix prototype used in this study. **Section 3** briefly discusses the 2019 novel coronavirus pandemic challenge from an EvoSysBio and a biodata science perspective – highlighting issues shared by all three grand research challenges. It also shows, how defining Landscapes of Incomplete Fitness Traits (LIFTs) can stimulate the study of Coronavirus evolution. **Section 4** uses the basic modeling principles of Section 2 for introducing two simple models about the nature of slow-motion explosions that are worth teaching to every human being capable of finding the log key on a pocket-calculator or searching the web for answering some basic arithmetic questions. We can only ignore these models at our own peril and the peril of those around us. Model 1 reveals easily whether efforts to diffuse the slow-motion explosion are working and how much time remains until ‘HalfMax’, here defined as the worst point, where the brunt of the pandemic hits. Since pandemics are a population problem that requires a population response, all humans as fundamentally rational beings need to learn enough about how slow-motion explosions work in order to convince *themselves* that it is worth their time and effort to actually fight the virus. Nobody else can do this for another person; hence the importance of readily available high-quality explanations for diverse audiences. Assuming a turn-around has been achieved and all behaviors stay the same, Model 2 makes it easy to predict when the ‘LastFive’ are reached and the deterministic power of the explosion can be broken by a dozen contact tracers; the model is mathematically not much different from predicting radioactive decay, yet to work it requires reasonably accurate reporting of new infections. **Section 5** constructs Model 3, or ‘PandemicSociety101’, which is a new adaptation of classical epidemiological models for investigating the current Coronavirus pandemic in light of much-debated questions. It enables several surprising conclusions by building on the modeling basics of Section 2. For example, it enables the observation of mortality rates for the case where all relevant details are known; it also allows us to show why herd-immunity is as good as non-existent for a virus that moves as fast as the Coronavirus in a population as susceptible as the US. The core of this model uses a new code motif for simulating a biological population (supporting a soft and a hard limit on its size); in turn, the core model itself is also a new code motif, albeit a much more specific one. It has been prepared for the extension of Model 3 into various other useful directions, such as the emergence of new virus mutants with specific Incomplete Fitness Traits (IFTs) that may affect the transmission of the virus (along with many other IFTs). Section 5 introduces Scenario 1, which asks how fast this virus might rip through a highly mobile country the size of the USA and how many deaths might result. **Section 6** discusses death traps that add to the death toll unnecessarily. Death rates are a complicated and mystifying. Measured in many more or less helpful ways, they remain remarkably diverse at all sorts of

scales. Here data from the US and the world is compared to the idealized Model 3 – only to find that the diversity of measures persist even if knowledge is perfect. Yet, our learning in response to the virus shows clear impacts on death rates at various levels. Thus, asking if this virus is ‘dangerous enough to care’ is as misguided as asking for precise progress every second in a 100m sprint – and if a medal worth the investment has already been earned. Section 6 also shows how limited testing facilities can easily lead to ‘linear fooling’, which is failure to grasp the fundamentally non-linear mathematical nature of slow-motion explosions – with devastating consequences. **Section 7** is the heart of this study and asks: what can we do beyond following now common advice and waiting for vaccines? Model 3 shows that a 289 million infection pandemic can in principle be shut down in mid-flight by sufficiently reducing the rates of shedding and catching of the virus. The factors required here appear to be within the realm of the possible. This is a pivotal and exciting insight from modeling that deserves widespread input from microbiological experiments and more detailed models in order to explore how fast and how much the respective rates of transmission can be driven down at what cost. Thus, this study raises the remarkable possibility that a pandemic as dangerous and as advanced as this one can still be shut-down by working clever together – without herd-immunity or vaccines – if we can manipulate key probabilities in the complex process we summarize as ‘infection’. The remainder of section 7 is dedicated to introducing and explaining a work-logic cascade with a mathematical structure similar to that of signal-transduction cascades from molecular biology. It shows how the human mind collectively can rule over microbes in principle, if there is (i) a reason to care for the hope and will to do so, (ii) the courage to balance on the edge of a sound mind that learns to choose well in what to trust, fear, or defy, and (iii) an unquestionable dedication to utterly submit to the truth and only the truth about the one reality we all live in (in contrast to committing to favorite models regardless of evidence, or trying to live with personally least inconvenient explanations) – which is next to worthless without a commitment to wrestling with the truth in whatever form it may present itself in order to find it to the best of ones knowledge-uncertainty within the given limitations (in contrast to fighting the truth, or being too credulous). The dynamics of this work-logic cascade suggest individuals can have an extraordinary input on the pandemic if they can find a suitable way to inspire by example and define consistent foundations for sound reasoning. The various levels of the cascade show surprising similarities that can be used to define respective LIFTs as introduced in EvoSysBio (see above). Since the work-logic cascade defines a strategy for winning against the pandemic, Section 7 amounts to a declaration of WWV. **Section 8** introduces ReRafts to accelerate the processing of pandemic-related data by improving batching strategies based on insights from re-designing Evolvix as a data language for biouncertainty in biodata science. Adequate batching strategies are essential for winning WWV and defusing various model-driven slow-motion explosions that impact data quality and that have been hampering pandemic responses. **Section 9** concludes with parallels to the causal probability network that sank the Titanic, aptly called a parable of our time. This warning is more serious than many realize; hence, it is explained in a bit more detail.

There is no religious denomination in which the misuse of metaphysical expressions has been responsible for so much sin as it has in mathematics {Wittgenstein, 1980 #27654}.

Counting. After two decades of professional work in computational, quantitative, systems ... biology a least inconvenient explanation of my publication record (REFs) would likely imply that I can count. Yet, for reasons beyond the scope of this study, at some point I had to face Reality and confess: I cannot count. My quest into aiming to better understand the numerical accuracy of the arithmetic operations that power so much of modern biology had led me to that point. By counting I do not mean the counting implied by most, which is merely repeating the execution of the so-called 'successor-function' (+1); I can do that; and I also do not mean the general human limitation of reliably executing anything precisely and without error for millions to times, even if as 'trivial' as adding +1. Neither do I mean my obviously deficient grasp of combinatorics, which can also be understood as an advanced method of counting. No, I mean something that is much simpler, yet harder since hidden: fundamentally understanding what counting really is, how to define it properly, how to avoid the numerous pitfalls along the way, and most importantly, how to arrive at a reasonable conclusion about 'what counts.' For example, I cannot even count the hairs on anybody's head; not because I miscount or cannot estimate how many there probably are (including sensible lower and upper limits); I cannot count the hairs on a head, because counting is something that is precise by definition, and when it comes to the mathematical precision of counting – easily grasped by the precision of counting the fingers on one's hand – then I have to admit, that I struggle with properly defining what it means to count the hairs on a head. I struggle as a computational biologist with growing interests in the logics required for defining a compiler for a general-purpose programming language for biology (which must, for example, define rigorous ways for handling the uncertainty in biodata). Probably, I would not see any difficulties if limited myself to biology alone (I'd likely fail to see most rigors of reliable counting) or computational logic alone (I'd likely underestimate the challenges posed the diversity of hairs on heads). Before allowing itself to conclude that $1+1=2$, for hundreds of pages *Principia Mathematica* presents proofs and conditions for ruling out structurally inconsistent notions, not few of which have to hold if counting is to be rigorous (REF). We will return to precise counting later; for now we only note that '*what really counts*' is an expression that may equally stand for the proofs and conditions mathematics requires for reliable counting, or the answer to the metaphysical question about '*the meaning of life*' (widely known to be '42', based on a famous computational model that struggled to document what counts; REF).

Counting in a pandemic. One might think that after a confirmed COVID-19 infection, counting the dead and those recovered will be the least of problems in the nation that led the world into the information age. The ability to confirm a new asymptomatic infection case from a new virus pandemic is a huge technological feat and by no means trivial. However, counting what happens afterwards seems even more complicated, even though only 2 eventual outcomes appear possible: recovery (i.e. a person presumably knows they are no longer infectious) or death

(there is a body). Without special degrees in ‘pre-pandemic smartphone culture’ many students from future generations will probably bet that the least of our current pandemic struggles is counting the dead (as there is a body) and counting those who are no longer infectious and feel recovered (even if imperfectly). Surely, in a society with smartphones that exceed what supercomputers could do in the early 1990’s, someone would have used blockchain technology to write a privacy protecting smart-phone app that simplifies for everybody the confirming of identify and declaring infection status without any fears of repercussions. Integrating counts in safe, independent, and not-for-profit clouds would simplify the counting so much, that not having it in common use by mid 2020 will strike future students as unbelievable – especially after years of clear and well documented warnings about the threat from new pandemics (e.g. REF film 2011+1 paper). It might seem as hard to believe as the official finding that in the last 24h before it sank, the Titanic received 6 specific warnings of the icefield it was heading towards at full speed. Yet, telegraphs were new and busy machines back then, because many of the important passengers had urgent messages to send and receive; thus, unfortunately, none of those 6 critically important warnings actually made it to the commando-bridge, where they should have been clearly visible for all who steered the ship. Our smart-phone cloud infrastructure might serve the COVID-19 core counting needs of the whole US faster than the many calculations it takes to serve the “right” ads for a single website visit. Yet, when impressions have become everything, the competition-bubble funds businesses that exploit common goods instead building them up, and basic research funding prefers highly competitive proposals in well-established fields, then the freedom of research required for developing useful software for fighting pandemics is squashed unless lucky accidents can link it to more ‘competitive’ ideas. It is not known why exactly not even US states like California and Massachusetts, home to world-leading universities and centers of innovation like the Silicon Valley, seem to be unable to count how many confirmed cases of COVID-19 have recovered. Fortunately, they report confirmed infections and deaths, so they likely have been trying to count the recovered too, but somehow seem to be unable find a reasonably accurate way to represent the uncertainty in their information – presumably because developing a system for doing so was not seen as ‘competitive enough’ to deserve funding at an earlier time if someone indeed had thought that this might be worth doing (whether this is the true cause or not is likely unknowable, because likely the development of such a system was self-censored by those who could have done it, but deemed it unfundable at the time). Decision-makers in such states simply draw the worst possible conclusion as they are overwhelmed by the biuncertainty in their datasets: they report nothing at all. While explicitly claiming ignorance, from a formal analysis point of view their claim cannot distinguish between the nuanced scenario above and outlandish nonsense such as ‘nobody in those states has yet recovered’ or ‘all who recovered were kidnapped by aliens before anybody knew. Of course, we would all like to report accurate and precise information, especially on such important occasions as this one. However, we also have to live within the means of our ability for accuracy and precision by openly sharing the knowledge-uncertainty attached to

our observations and conclusions. There exists no general-purpose data language that can handle the ubiquitous biouncertainty that comes with biodata and is on full display in this pandemic for anybody who attempts to get to almost any accurate and precise count of any quantity of general interest. Those who report data for recovered are not much better in that respect, because they do not report the biouncertainty underpinning their counts that appear perfectly precise (yet are bound to have credible upper or lower limits). However, consciously or not, those who report their imperfect data have resisted the '*rounding error of hopelessness*' by deciding to share their small contributions and not withhold them. This rounding error of hopelessness is dangerous, because it can withhold myriad small actions that cannot individually change a big picture, yet can do it in combination; however, if each individual who could contribute decides that it's 'not worth doing', because they 'cannot make enough of a difference', 'have no hope of getting it right', 'do not want to share their state of confusion', or any other reason, then a big terrible outcome might become inevitable – even though collective action could have easily prevented it. Considerations like these have motivated this study and are motivating the ongoing efforts to develop Evolvix into a general-purpose computer language designed for biology, which must include robust abilities for handling the biouncertainty in all its calculations properly and out of the box. More about Evolvix later.

Counting in non-linear worlds. When Newton discovered linear calculus, he gave us an astonishingly powerful tool for understanding what nature does. It cannot explain everything, but it is easy to understand why someone introduced to its full predictive powers might think that it can. Its power is in providing a formal system for calculating with quantities in a linear world, which previously may have been accessible by intuition – for those lucky to have the right one. Newton found a way to teach those who did not happen to already have the right intuition, how to develop one (if willing to brave the notation and invest the time). The advantage of such formal systems is that every step of an analysis can be broken down into all its sub-steps, down to the simplest possible instructions, such that even computers can behave as if they understood it – simply by following the stack of rules that define it. While this stack of rules for linear calculus is surprisingly useful for describing and predicting many linear processes of real-world interest, most of us can easily live without it, since we have a reasonably thorough intuitive grasp on the linear world into which we are born. Time, space, mass, energy, and many other derived quantities scale linearly and our intuitive grasp of the respective calculus allow us to average and integrate effortlessly. For example, if we have a heap of sand we aim to move with a shovel and a cart, and it takes us 1h to move 1 ton of it to its new place, most have no difficulty predicting that it will take 5h to move 5 tons if all conditions stay the same – no calculus course needed. What a formal calculus allows us to do in this scenario is to efficiently handle many potential variations and reliably predict in light of available data, e.g. how much we might move if the sand has to go to different locations, or different carts allow for different speeds, and so on. Thus, we can make responsible decisions without a need for calculus by combining our intuitive grasp of it with our intuitive grasp of how to handle uncertainty in a reasonable

way (i.e. by leaving some slack in the system and not creating impossible double-binds by overcommitting to transport sand to places we could not possibly ever reach in time). A detailed calculus allows us to improve our predictions, and thus to reduce the slack we'd otherwise have to leave in order to stay on track and avoid over-committing. While ongoing, such a calculus also allows us to track progress towards milestones of interest, such as completing the task. All well and nice so far, but why discuss calculus in a study of the coronavirus? As it turns out, Newton's linear calculus – while being the first to be discovered, the simplest, and in many ways the most foundational one – is not the only calculus that exists. Here I am not referring to advanced process calculi for modeling concurrent processes (e.g. ref to pi calculus and BioPEPA) or for logic calculi for general computing (e.g. ref to lambda calculus). I am referring to the work in the area of 'non-linear calculus' {Grossman, 2020-06-28 #29034; Grossman, 1972 #29035; Grossman, 1980 #29037; Grossman, 1983 #29038} and in particular the multiplicative calculus {Grossman, 1979 #29036; Bashirov, 2008 #29040}. It is best used in a world, where addition and subtraction (the basic operations of the linear calculus) are replaced by multiplication and division as new basic operations. While such a world is more restricted than our linear world, where values can become negative, it turns out to be an excellent description of the world of growing populations (that rise by multiplying the number of parents by the offspring each produces) or the world of decaying left-overs (such as radioactive decay that removes a constant fraction over a constant linear time-interval).

It turns out that the aspects of the Coronavirus that really matter live in a multiplicative world and not in our linear one; they have eventually an impact on our linear world, but they are driven by their own multiplicative world. Thus, in order to understand what happens next, we require insights and intuitions about that multiplicative world in order to understand what happens next in our linear world. Without such understanding we are likely to walk into a trap. Unfortunately, this trap of misunderstanding is complex, abstract, and largely invisible; it involves aspects of measure theory that must not be mishandled, yet easily are, especially by biologists without the necessary mathematical background and sufficient intuitive experience from years of exercise. Further details are explained in an introduction to measurement theory for biologists {Houle, 2011 #8558} and include how to pay attention to the theoretical context of the underpinning real-world biology, which is essential for appropriately reporting relevant data, refraining from misleading transformations, and accurately estimating relevant uncertainties. These authors found important principles to be frequently violated in biological data analyses {Houle, 2011 #8558}; this likely contributes to the already sizeable cost of irreproducibility in biological data analyses {Freedman, 2015 #9665}. The calls for more rigorous quantitative training and better reproducibility are echoed here, because both are important; however, given my own experience, I would like to point out that the complex nature of these abstractions requires a much more fundamental reorientation of research and teaching, before large-scale improvements of reproducibility and reliability can be realized in biological research. Here is not the space for a proper introduction to an approach that stands a chance of achieving this, hence a brief

sketch must suffice. Analyses of human error rates have shown that these keep rising as the number of logical conditions increase that have to be tracked consciously; thus, the problem exists even in the best case (we know all relevant rules); however, learning enough statistics, measure theory, and related disciplines for addressing these error problems is not possible without seriously detracting pivotal attention from biological research questions; thus, putting it at odds with the interest of biologists to study biology. In order to appropriately solve these challenges without spinning educational- and research-wheels in the sand, we need a compiler for a long-term stable extensible user-friendly data and modeling language for biologists, that knows all the rules, integrates them in the best way for widespread use in teaching, and allows researchers to extend them as they uncover new special cases in the analyses of real-world systems. We need the resulting library of statistical logic operations that select the best-of-breed methods for analyzing a particular case, implements corresponding work-flow templates, and auto-generates concise reports of all relevant knowledge-uncertainty limits associated with an analysis. Expecting biological research to learn how to use such a compiler well (if sufficiently stable and user-friendly), pay attention to warnings it produces, and know where to ask for help as needed, that is a reasonable expectation for someone dedicated to exploring biology; expecting the same biologists to essentially acquire all statistical domain expertise required for writing the functions of that compiler that they would use if it existed, that is an impossible expectation; it lays much undeserved implicit guilt on those who cannot know much better if they stay true to their focus on biology. The real problem is that our current research ecosystem does not really support those well who wish to write tools that serve generally acknowledged common goods and that would make everybody's life easier; a similar problem is known to open-source software developers who are also frequently threatened with starvation if they stay true to their mission.

#MyGuilt. To illustrate the difficulty of intuitively anticipating important and obvious consequences in a non-linear world, it is instructive to review a few milestones of my own introduction to it and my ability to leverage them. I learned about exponential growth too long ago in school to remember it. As a biology undergraduate I was introduced to the importance of r and K in the classical model of a new stable population, such as one that might result from arriving at a new empty island, where it grows at rate r until K individuals fill the island. I realized that r and the Doubling Time DT are related. During my dissertation research I measured high-precision growth curves of such stationary bacterial populations in order to observe the effects sizes of deleterious mutation accumulation (REF),

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4 Mission Impossible: Timers to stop a slow-motion explosion

4.1 HalfMax clock: a rough timer for the brunt of a slow-motion explosion

4.2 LastFive clock: a rough timer for defusing a slow-motion explosion

Show what to enter in R + simple equations for pocket calculators

4.3 Comparisons to observations in the US up to May 2020

Exploring WHAT-IF Scenarios in the Computer: Simple Forecasting of Knowledge-Uncertainty on the SLOW-MOTION EXPLOSION of US Coronavirus Infections

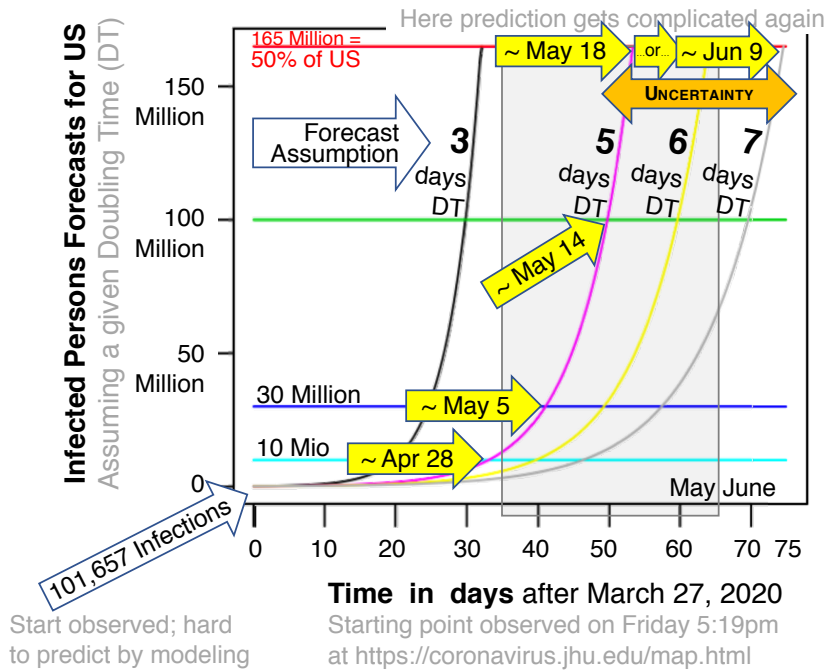
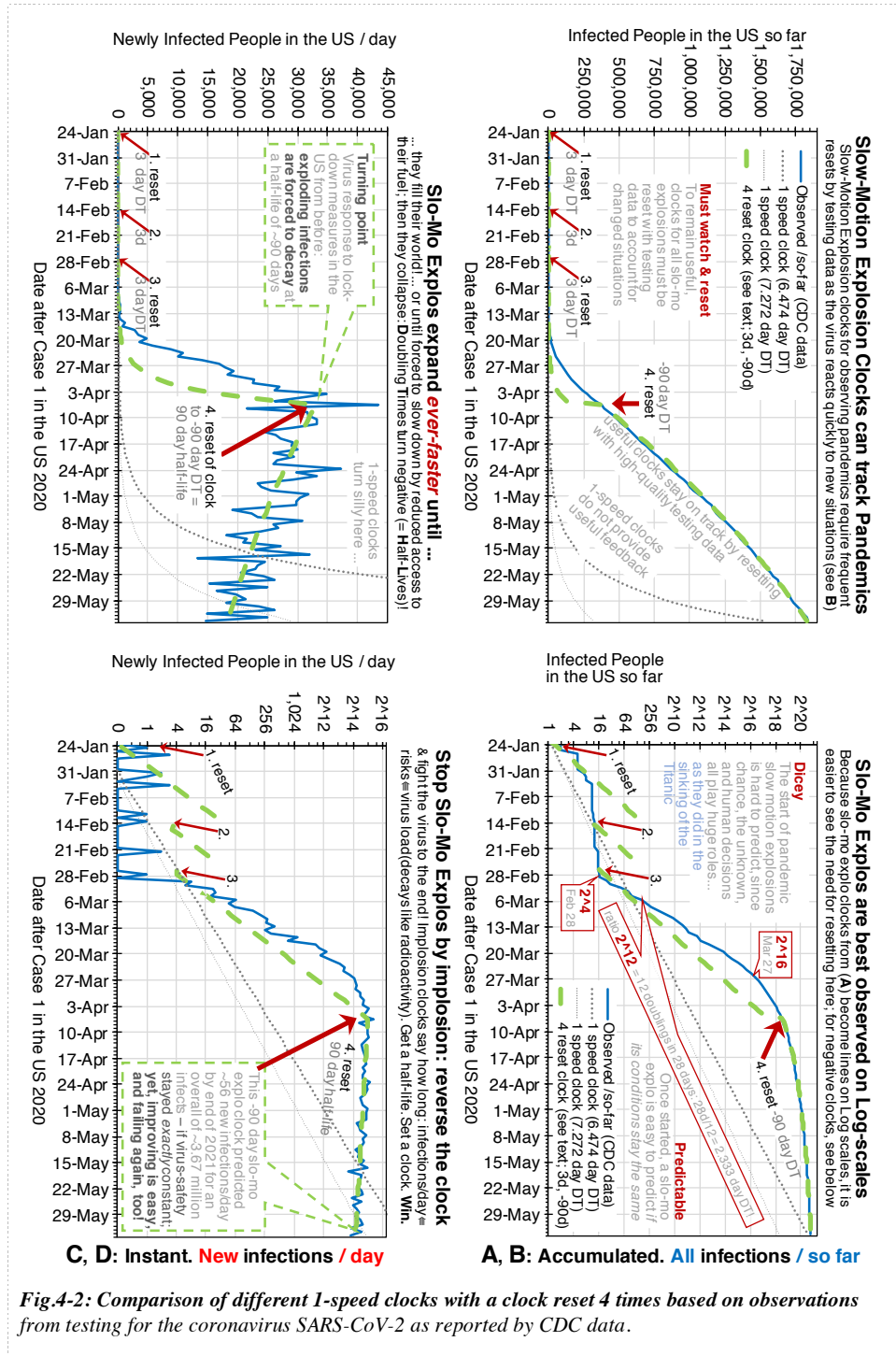


Fig.4-1: The ‘brunt’ of this slo-mo explo is defined as ‘HalfMax’, the point in time, when half of the population will be infected with a completely novel virus that multiplies fast enough to rip through the whole population without giving it a chance to develop any herd-immunity worth noting. Thus, HalfMax for this pandemic for all of the US is 165 million infections. These early prognoses are kept as a reminder where the US would have been without any change in behavior. These Model-1 prediction assume no changes in behavior whatsoever, and thus require frequent calibration; however, human behavior is so complicated, that it is probably more straightforward to use simple “continue as is” predictions like these and frequently adjust them, than to try to use a model that tries to include in its predictions human behavior itself (by comparison, the work-logic cascade discussed later has much more modest goals than would be required for predicting the daily number of infections correctly). The line at the top (where it “gets complicated again”) indicates that this model ends there, even if human behavior was constant.



5 PandemicSociety101: an advanced SIR model that is more realistic

After introducing the extremely crude slow-motion explosion model above, it is now time to add more details which are known to matter for pandemics. For example, Model 1 above assumes that a pandemic has already started and keeps growing, while Model 2 assumes that a pandemic is already ending and merely uses its half-life to calculate an expected end date. However, neither of these can address how the transition might come about. To answer this question experts have developed a type of model also known as a SIR model, where susceptible individuals can meet infected individuals and thereby get infected until the infection ends and they are removed from the epidemic in the model. A great many variants of SIR-model exist (REFs) and have also been used for understanding this 2019 coronavirus pandemic. In that sense the model presented below is not particularly new, however, it provides some useful additional insights into questions that continue to be discussed. These include mortality rates, how much testing is enough, whether herd-immunity can help, and most important of all, if there is a possibility to stop this pandemic without the need of vaccines. In addition, this more sophisticated model allows us to test the limits of our much simpler slow-motion explosion timer models above. These models matter because they can allow a middle-school student to make important predictions about a pandemic with a pocket calculator -- if they know how to interpret the model and where its limits are. In contrast, the following advanced SIR-model requires more expertise to use than is currently widespread. As we will see, for a number of scenarios the simple model works well and there is no need for complicated modeling in order to make responsible decisions. As we will also see, there are many detailed scenarios where the simple models are not enough. This current model can shed a little more insight, but to really answer the questions much more extensive modeling and data-gathering is required than this study (or even a sizable institution) can accomplish. Towards the end we will return to the question of how these models can be built and used in order to accomplish what currently seems impossible according to informed public sentiment and comment from experts: getting rid of the 2019 Coronavirus. This is not to imply that the task is easy (it is not) nor that it is possible (impossible to know at this time). However, as we will see, this study implies that despite over 2 million infections in the U.S. and over 9 million worldwide (REF check #s), there is a small chance that humanity can still launch a successful worldwide war against the Coronavirus, and thereby prevent unspeakable mountains of misery, save many good parts of our civilization, let go of less helpful practices, while simultaneously laying the foundations for a worldwide culture of innovation and research that values the equality of human dignity. However, before returning to these questions, let's revisit some basics of what we know about the Coronavirus and Covid-19, the disease it causes. This is efficiently done in the form of a model.

5.1 Overview of the PandemicSociety101 model for the Evolvix prototype



5.2 Comparison of PandemicSociety101 to typical SIR models

5.5 Overview of ‘back to normal’ Scenario 1 in PandemicSociety101

5.5.1 Choosing values for the Input Parameter Use Table: Scenario 1 InPUT

5.5.2 Deterministic (ODE) and Stochastic (SSA) OutPUT for Scenario 1

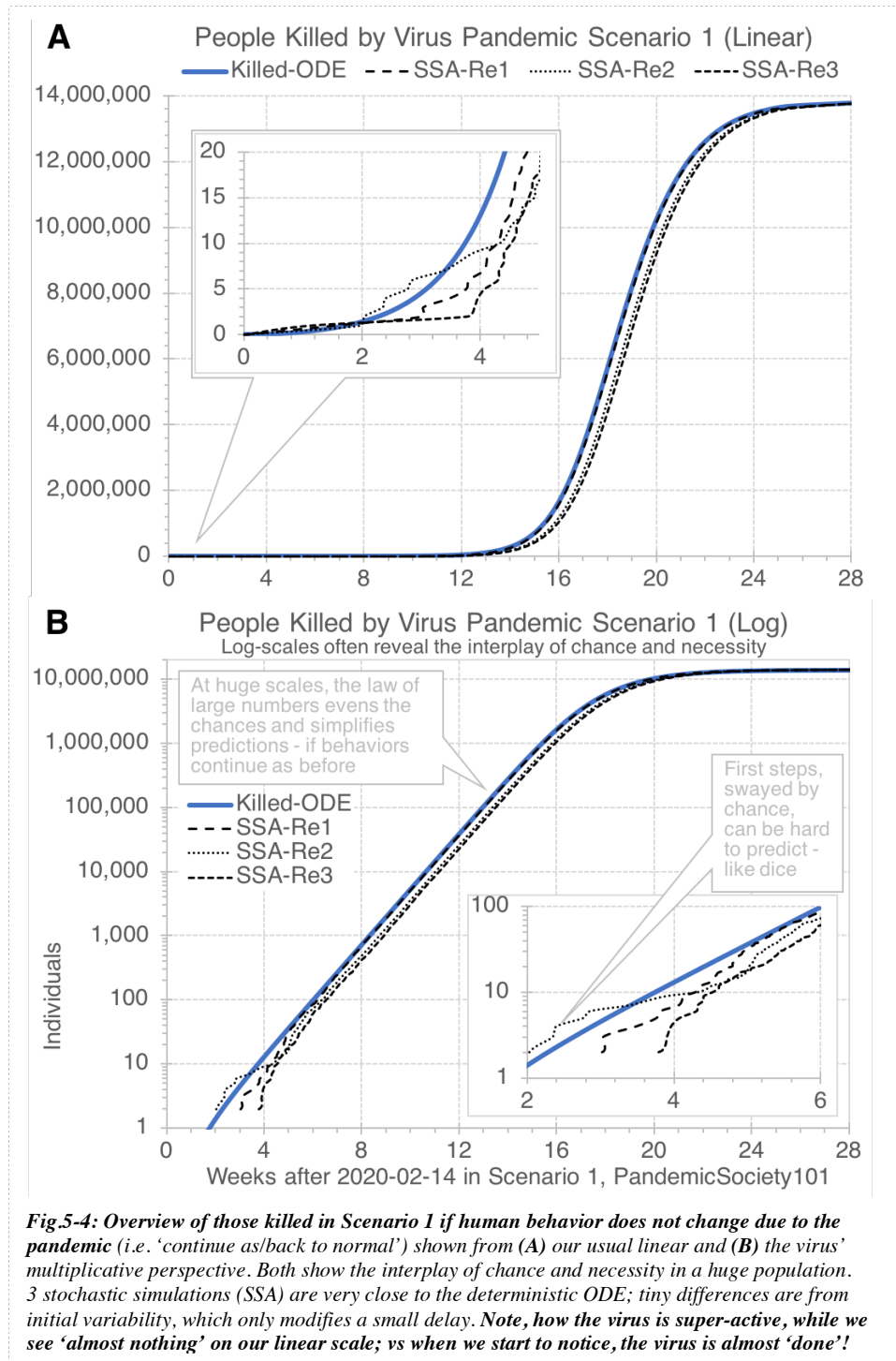
Fig.5-4:

5.5.3 Overview of the core OutPUT for Scenario 1 PandemicSociety101

Fig.5-5:

5.5.4 Why the simple SloMoExplo timers are surprisingly useful

5.5.5 Pragmatic approach taken to InPUT for Scenario 1



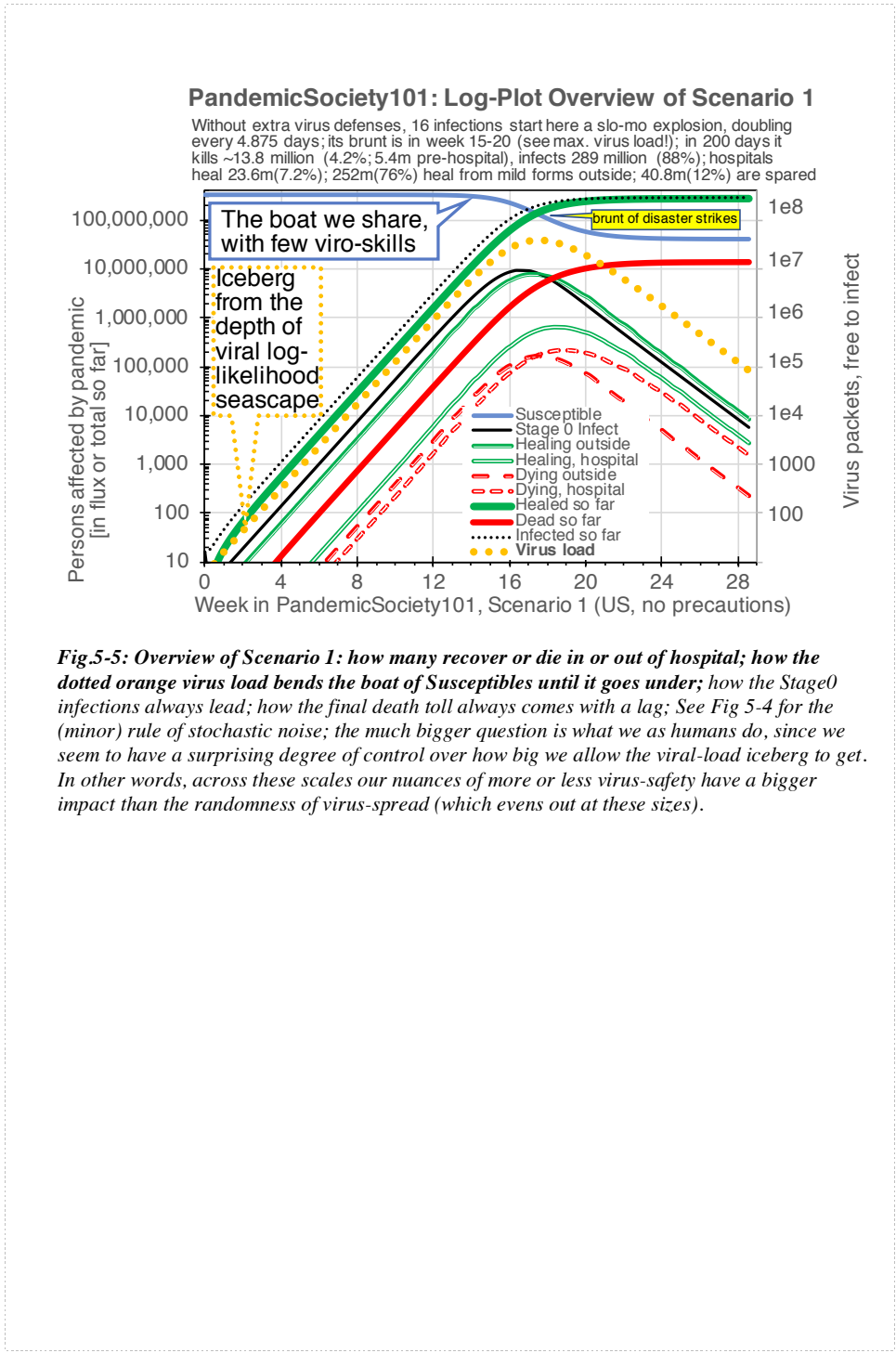


Fig 5-5: Overview of Scenario 1: how many recover or die in or out of hospital; how the dotted orange virus load bends the boat of Susceptibles until it goes under; how the Stage0 infections always lead; how the final death toll always comes with a lag; See Fig 5-4 for the (minor) rule of stochastic noise; the much bigger question is what we as humans do, since we seem to have a surprising degree of control over how big we allow the viral-load iceberg to get. In other words, across these scales our nuances of more or less virus-safety have a bigger impact than the randomness of virus-spread (which evens out at these sizes).

6 Pandemic Death Traps to watch out for

6.1 Expecting death to follow simple rules

6.1.1 Why are mortality rates so complicated? – decision-making & learning

6.1.2 PandemicSociety101: Mortality rates when ‘everything’ is known.

6.1.3 How DoR DoC mortality rates might vary across states in the USA

6.1.4 How DoR DoC mortality rates might vary internationally

6.1.5 Surprising problems with mortality rates

6.1.6 Why mortality rates matter less and matter more than some think

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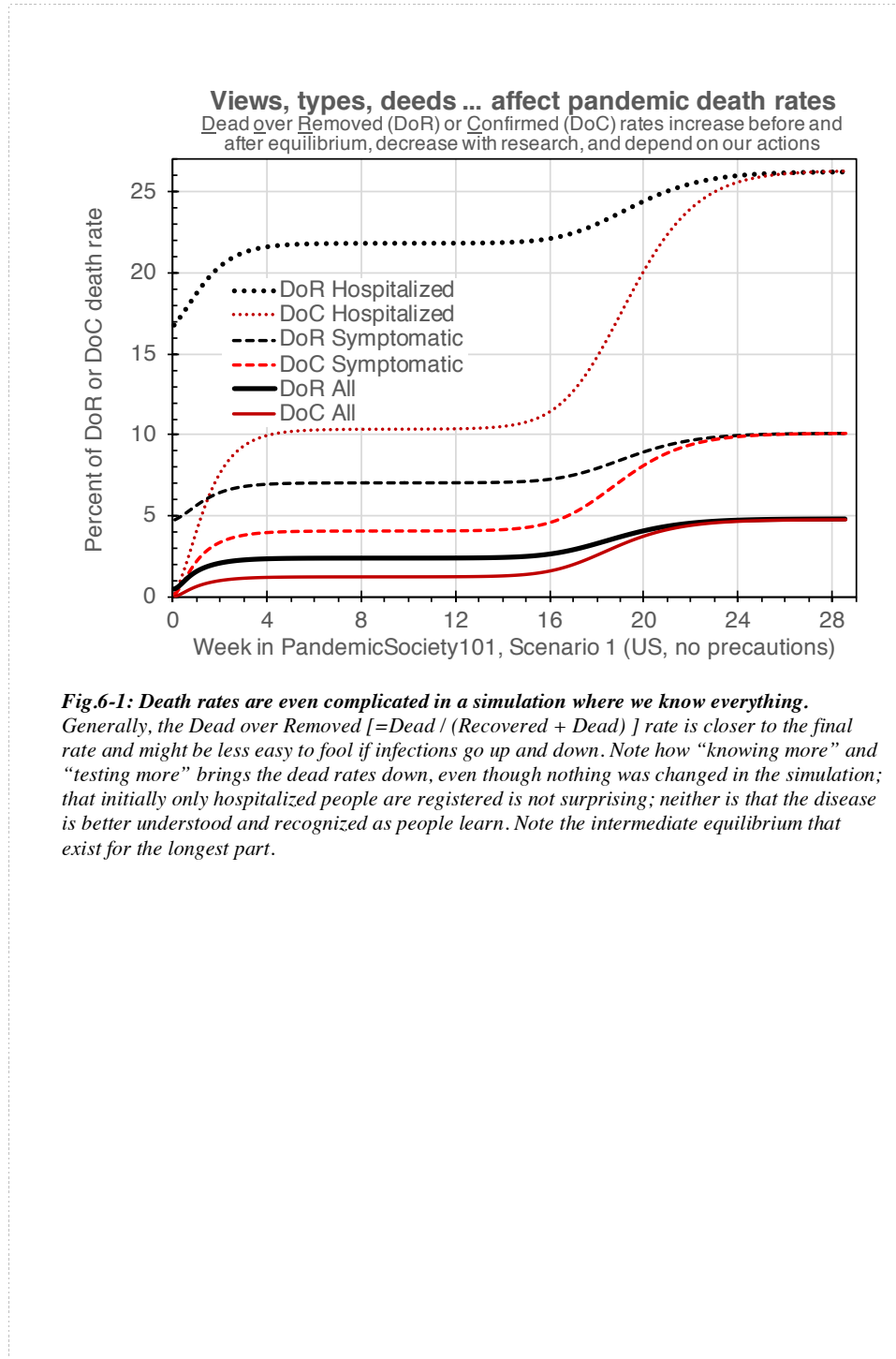
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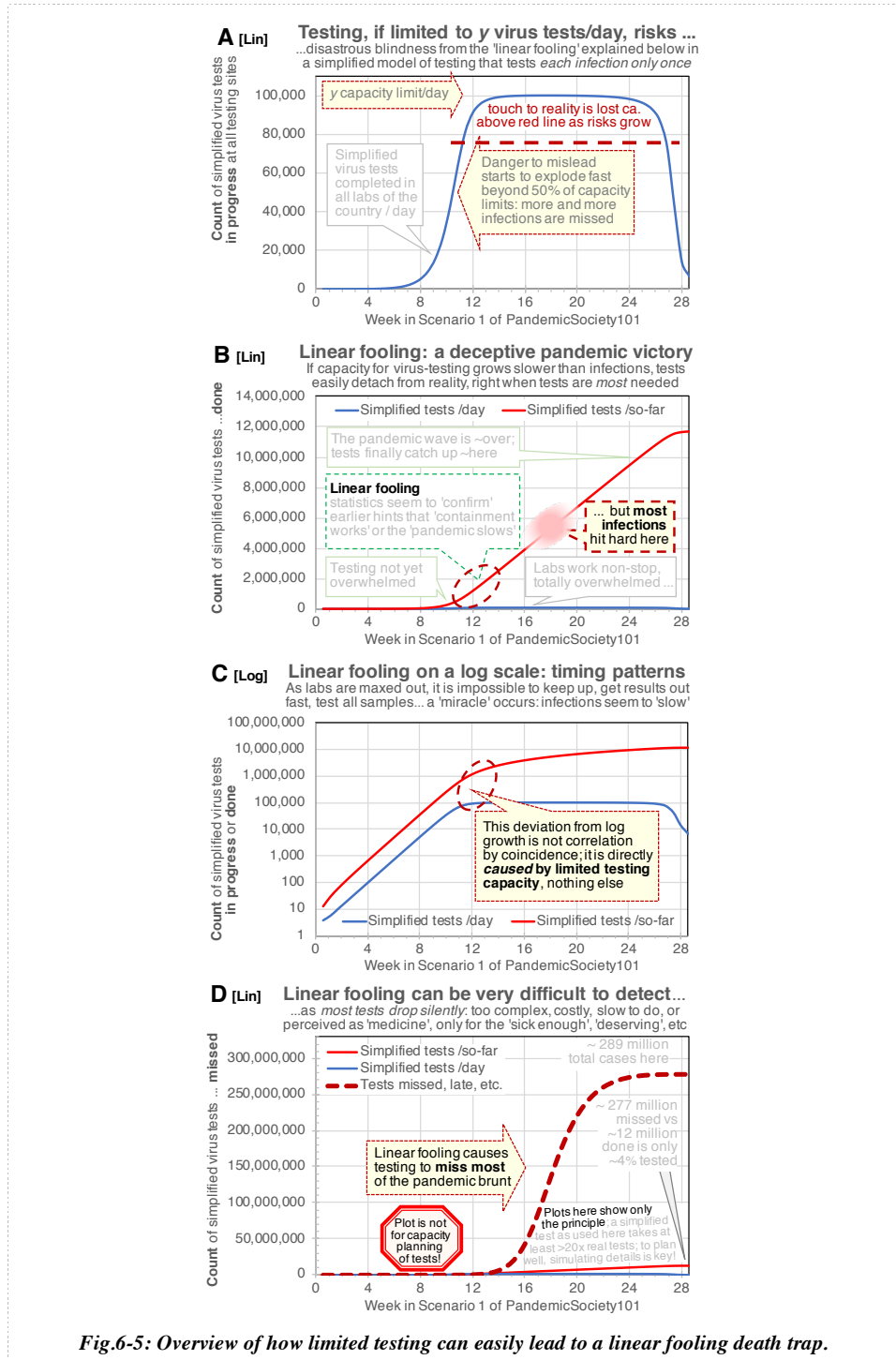


Fig.6-5: Overview of how limited testing can easily lead to a linear fooling death trap.

7 A fool's hope: Stopping this pandemic without a vaccine

7.1 Reality leaves a lot to our imagination.

7.2 On the rounding error of hopelessness

7.3 How to stop this pandemic? – Microbiology

7.4 How to stop this pandemic? – Mental approaches LIFT

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7.9 How to stop this pandemic? – Taking World War V seriously, but how?

PandemicSociety101, Scenario 2: The Next Defense

The pandemic's future is still wide open. Most of it depends on the option chosen:

A: Half 0: go 'back to normal', no cuts to virus drop or catch, DT 4.8d (Scenario 1)

B: Half 1: 50% lower probability of dropping or catching the virus, brings big benefits

C: Half 2: 50% lower probability of *both* dropping and catching viruses. **It all stops.**

If facemasks aid C, can we ignite a culture of inventing fashionable facemasks?

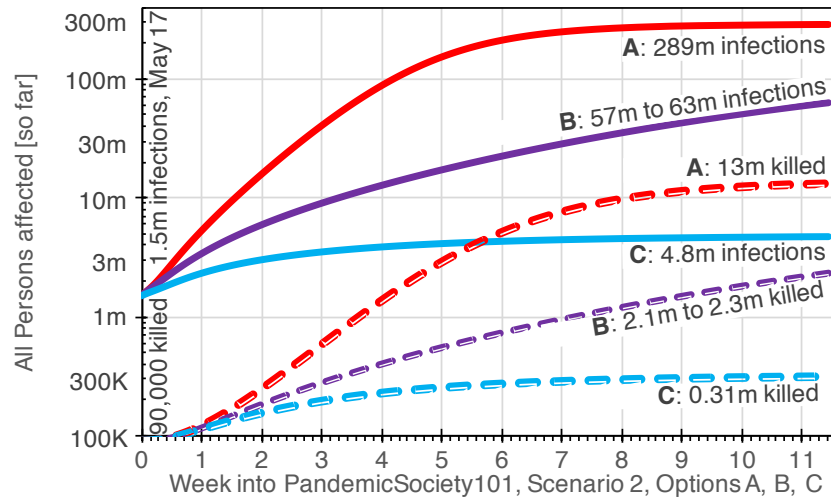
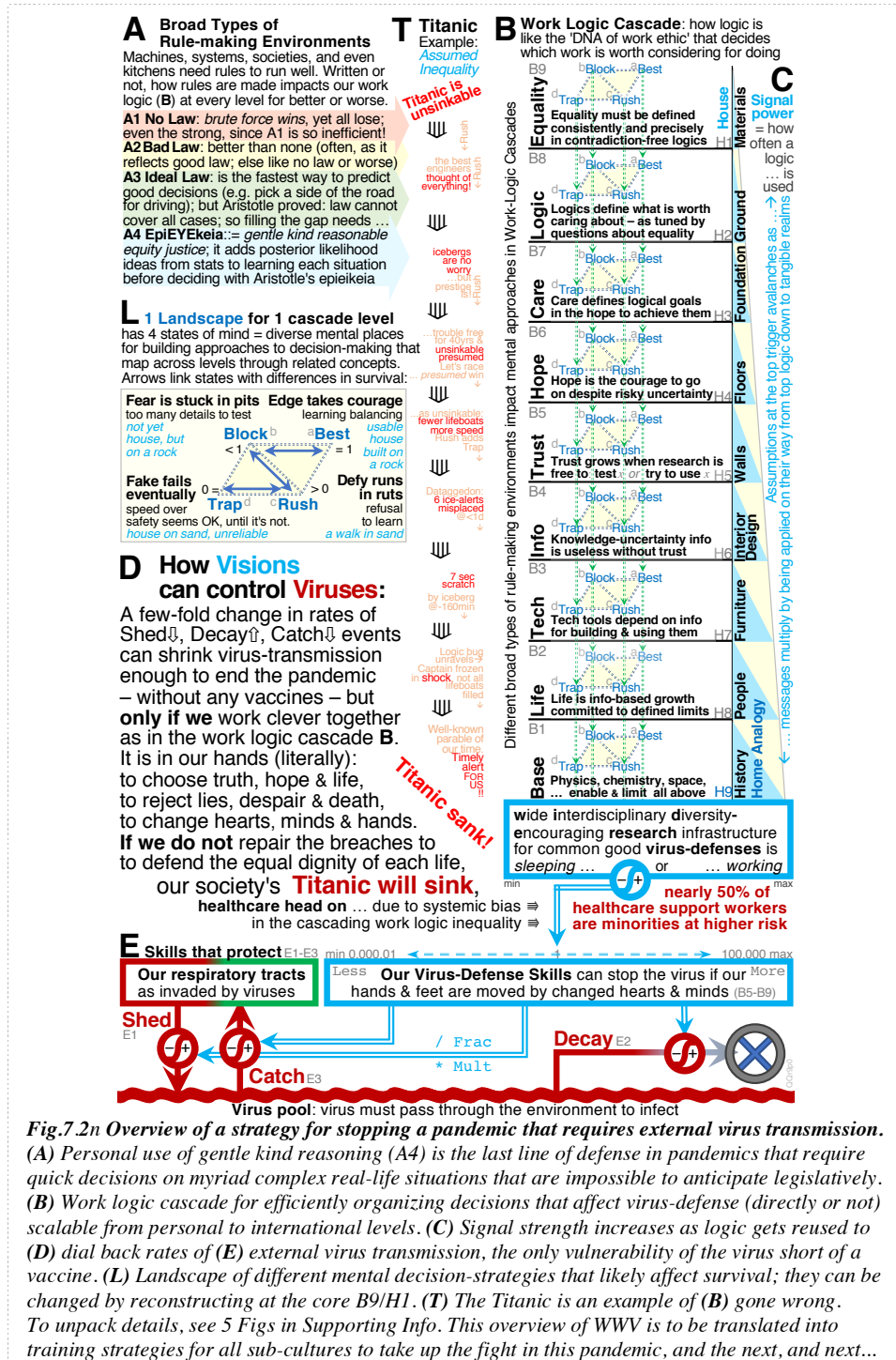


Fig.7-1: Overview of a key proof of existence of a fool's hope of stopping this pandemic in mid-flight. This fool's hope would not exist, if it was impossible to show for biologically reasonable parameter combinations in Model 3 that seemingly realistic manipulations of probabilities for shedding, decaying, or catching the virus could actually stop the pandemic. Phew – why so many negations? Is it not fair to say that this shows that it can be done? Actually, no. It is fair to say that these results suggest it might be possible; however, we do not know enough to guarantee it. Given the enormous costs of 'lockdown', it is worth collating a more complete picture across the multitudes of daily-life scenarios across the nation. Doing so to reach reliable conclusions requires much more data integration, microbiology experiments, statistical logic, simulations, and biodata science than any single lab (or even institution) could do. To facilitate the fastest possible start for those willing to explore this fool's hope, the simulation code and simulator have been made available in a ReRaft – and ReRafts are being developed as a reasoning strategy to figure this puzzle out: can we actually still stop the coronavirus in mid-flight without forcing everybody to stay home all the time? It is not clear if we can, albeit allowing this killer to walk all over the US without exploring every potential loophole left to stop it, that seems like a pro-death position.



8. ReRafts for fighting the data tsunamis that feed the infodemic

8.1 The effects on data tsunamis in biology are huge but not easy to detect

8.2 ReRafts: the core batching idea in overview

8.3 ReRafts must first prove their value as life-savers for research efforts

Defining the ReRaft Mission and Vision

8.4 HUMAN MACHINE Negotiations and batching efficiency

8.5 Overview of a Data-Oriented-Insight-Storage-Architecture

8.6 Overview of features that matter across all scales: FAIR-VIEWABLE

8.7 Overview of a population genomics perspective on improving code-bases

8.8 Overview of Stabilizing yet Versioning perspectives for individual insights

Defining the ReRaft Mission and Vision

The ReRaft idea has been growing with the challenges presented by biodata. It aims to define types for reducing the struggle to make biodata work seamlessly across biology. Metaphorically, the rules for ReRaft types define answers for the question on ‘which side of the road to drive’ if Alice and Bob keep exchanging different yet related data sets in order to efficiently reason about their meaning. Thus, ReRaft types aim to reduce confusion, which places stringent requirements on their development and on how they can address the confusion and uncertainty they otherwise imply. ReRafts seek to find reasonable and workable long-term solutions to these problems that arise when handling the extreme diversity of biouncertainty data while aiming minimizing loss of accuracy from wanton exclusion of most data (and thereby much increasing uncontrolled biases). Such efforts rise in importance as biology approaches a time when it produces more big data by volume than classical sources of big data (REF Genomical).

ReRafts is an acronym supported by this Vision, Mission, and Definition:

Research Encouraging Resilient Adaptable Filing Transporter System.

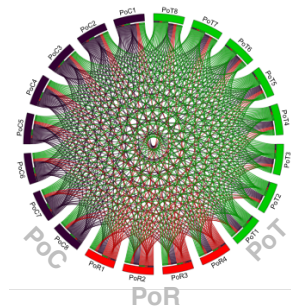
Vision: *ReRafts are life rafts for saving research efforts in floods of data.*

Mission: *Improve type systems for protecting relevant information from oblivion, for reviewing reliability, and for stabilizing FAIR-VIEWABLE insights.*

Definition: *ReRafts are versioned processing points for data flows that simplify reliability testing by following the rules of a well-defined ReRaft type.*

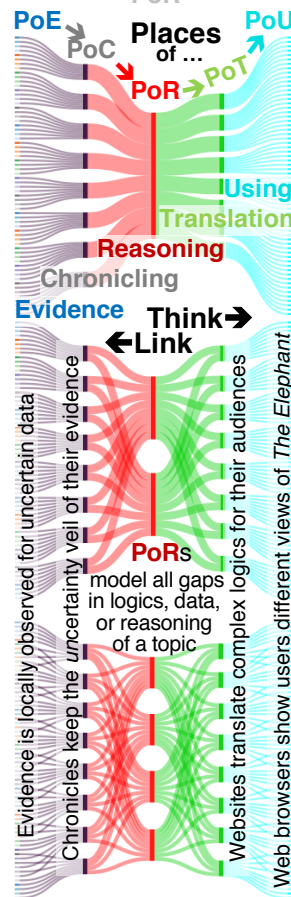
ReRafts are being developed as part of the Evolvix effort to define a century-stable computer-language for biology. Evolvix work so far has shown (REFs) that any efficient simulation system for biology will also require a flexible and easily accessible data storage solution of outstanding stability if it is not to waste the time of their users.

8.2 ReRafts: the core batching idea in overview



A Info-Jungle flows in any direction

Lack of site types, chaotic reasoning, and wild formatting makes fact-checking slow, costly, & error-prone – like searching a swampy labyrinth.



B ReRaft types can organize info-flow

Imagine ... websites declare the type of info-place they want to be, link to sources, and assist users who test their conclusions. How much info-noise would simply vanish?

C Alternative logic is easily included

No need for universal agreement if another logic can be justified: new PoRs can argue new views; yet quality is to be tested with a system that rewards: add quality, cut bugs!

D Distributed work can be batched

Imagine ... cut global data quality costs for testing and reasoning by efficiently batching declared types that are easy to check if in doubt. A few sites

competing in transparent ways for quality will cover their scope better at less cost than myriad mediocre pieces – liberating research time for new questions!

Fig.8-2: ReRafts can greatly cut the cost of keeping up to date via batching. This works well, as long as reliable mechanisms for testing the quality of insights are readily available, else not.

8.4 **HU**man **MA**chine **Ne**gotiations and batching efficiency

As explained above, post-genomic biology has demonstrated, how batching similar tasks into groups can enable efficiencies of scale that enable entirely new questions to come into view. To get there efficiently for biodata science, it is pivotal to realize what may seem trivial for rescue-workers and cleanup-operations in disaster-struck zones such as a tsunami aftermath: we need an efficient collaboration between skilled experts, local volunteers, and machines. In order to optimize this collaboration, we need the special type of negotiation defined in Fig.8-4.

HU man	EpiEYEkeia: great, but no point in reinventing what experience says can be encoded with a logic that can generalize common experiences without overcomplicating the rules for everybody; identify rules that don't work.
MA chine	Rules, can be too brittle, eg. unbending rules that crash planes into the ground; but MAChines are great at error-checking and repetitive rule-execution.
Ne gotiations	Teach MAChines, use MAChines, improve quality of rule-defining environment

Fig.8-4: Humans and machines have strength and weaknesses that complement each other to a surprising degree. To maximize innovation and pandemic safety, it is essential that we understand each well and learn of to negotiate the spectrum of biodata science tasks much more efficiently. It turns out that freedom of research is essential for avoiding a long list of needless complications.

Such work requires a better interface for such HU MA Negotiation with respect to the well-known logical operators 'and', 'or', which are much more confusing than widely appreciated.

8.4.1 (was 2.5) Logics, the witches of andOr, and virus-safety

Fig.2-4. The price for elegance and brevity as extracted by the witches of andOr: confusion. There are surprising amounts of confusion surrounding even "simple" logical operations like BooleanAnd, BooleanOr, as often represented by 'and', 'or', as respective English words. The worst part of this confusion is that most often even usually well-informed people are not aware of the extent of confusion generated. While programmers happily converge on the traditional Boolean interpretations, not everybody else naturally sees it that way. Thus, complex conditional scenarios become challenging, such as increasingly likely required for virus-risk management. A few random examples are included for illustrative purposes; to be actually fully prepared for high-levels of virus-safety, a great number of conditions of daily life require matching with a growing number of papers that update general knowledge about how to handle the virus. This is just one application of andOr; many others persist. See the discussion of EvoSysBio for another.

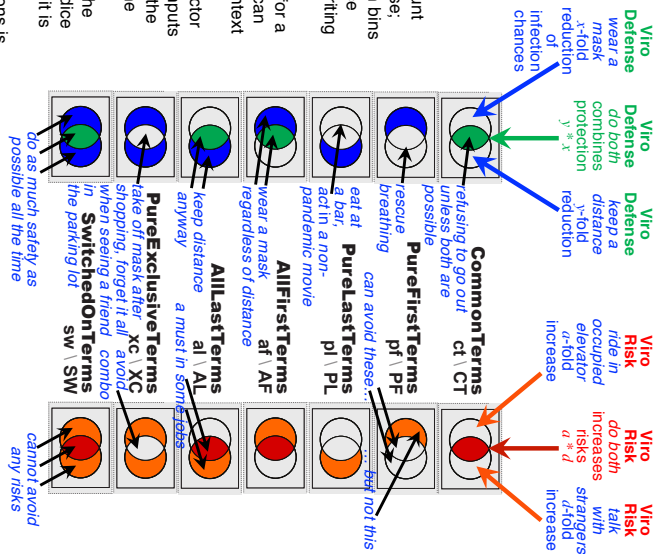
Respecting the Witches of andOr

Choosing 1 binary output from 2 binary inputs leads to exactly 16 output options. Of these, 7 reside in the land of 'andOr', which gets its name from the difficulties of distinguishing between "and" and "or" – or was it "and" or "or", or both, or only one of them, or any combination? To avoid the headaches of having to use "and/or", or "and", or "or", etc. and have to determine all correct options all the time (and often forget some), a logical operator is defined here that packages all the ambiguity into a big warning sign:

andOr ::= is defined as the deliberately ambiguous logical operator that can stand for any of the logical combinations displayed here, ranging from only 1 copy of *CommonTerms* (e.g. when conditions 'intersect') to each copies in the *SwitchedOnTerms* (e.g. as in the 'union' of all mentions).

The witches of andOr rearrange this operator internally so that only the correct combinations of all options count as correct use, while all incorrect options are silently dropped as non-existent. Incorrect options make no sense: they amount to false statements and are swept into *nothing* to be ignored (think of the big O in andOr as trash bins or zero black holes; that devour contradictory nonsense so it is gone). This disappearance generates elegance of writing; spelling out a long list of options that do not work is rarely liked by anyone. In return, the unusual writing is intended as a *reminder that all related logical analyses required for full clarity have merely been postponed*.

When postpone logical analyses? Reasons abound. Not all conditions might already be sufficiently known for a given andOr statement to allow its full resolution; it might be too complicated to go through all options, which can pile up quickly; conditions may include but are not limited to the context of the statement made, andOr so on. Complexity explodes quickly, when new conditions are independent and multiply all previous options with a factor that adds new options to each case considered before; also, conditions may change over time; more than 2 inputs may be chained; *CommonTerms* must never be counted twice in some contexts (e.g. in Boolean logic; law of the excluded middle), but other contexts demand it (e.g. when biology studies duplicates or near-duplicates). In the resulting networks of dependencies, not all combinations have to be valid, because the witches of andOr will always clean up – *even if it is too complicated for us to predict how*. In such cases, it may be tempting to roll the dice, since sufficiently complicated systems often appear random to those who do not understand them. Yet, dice are usually a mistake here, as the witches almost never roll the dice; they usually have good reasons, even if it is too hard for us to predict which of the myriad potential conditions apply. It is surprising how much complexity English can hide behind the simple words "and" andOr "or"! The price for the magic of these elegant incantations is in the painstaking work it takes to understand their meaning correctly. It can cost much time to pay full attention to which options actually count – yet it can also literally pay off: some deals use andOr in the more common forms "and", "or", to claim afterwards that a clearly existed, which eludes customers who do not analyze the fine print. There is almost no end to andOr complexity; add in "not" to get the core of a full programming language like Prolog. **In short:** Describing a logic puzzle (in English or Prolog) requires less thinking than solving it (in Mind or Machine). Thought is work. If "instant" wins, postponing wins. **But:** If results win, thought → training, brain → muscle. → **We win!**



Myriad daily life virus-defense cases wait to be understood ↔ described. Small logic puzzles (= programs) help to cut memory-load if we train our brain to respect everything andOr nothing

8.4.2 (was 3.2) *wid-e* Research complexity diversity has room for many minds

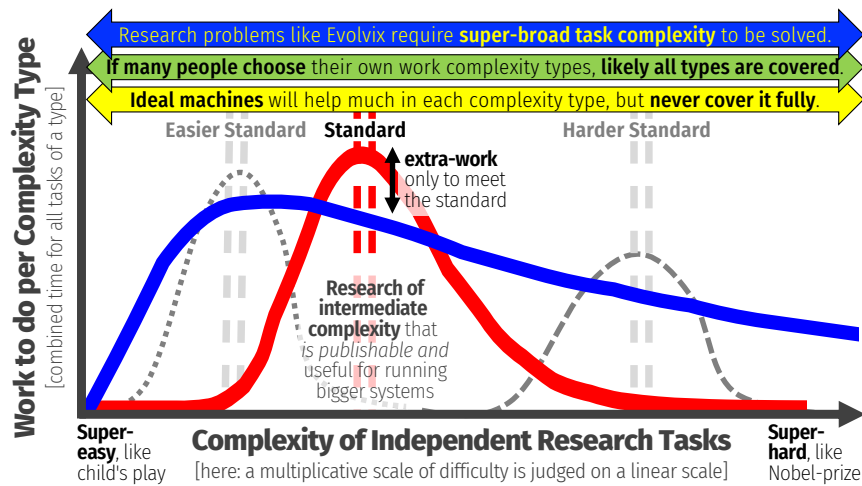


Fig.3-2: Overview of the complexity of research tasks on a log-scale. Initially developed for better understanding the diversity of challenges in developing Evolvix, it turns out that research for stopping the Coronavirus is not much different in principle (as are many other challenging problems of our time); these do not tend to ask for permission before crossing challenging disciplinary boundaries. They just do. The tasks in this diagram that can be addressed right away by *wid-e* research are the small ones at the beginning, all others require a longer-term ram-up time. For example, developing a well-working vaccine against the coronavirus in record time and by addressing fundamental new biological challenges due to the nature of the virus may well earn someone a Nobel prize; however, those who stand a chance of doing such work, are likely already working on it (or at least know that they could). Everybody else is likely more productive (and happier) with smaller tasks; the incentive-structure of modern research universities focuses on intermediate complexity; however, COVID-19 research has also shown that there are mountains of smaller tasks of equal importance to the overall success of beating the virus: Reliable data integration requires a chunk of understanding and maintaining it well in light of all ongoing updates; machine-learning will struggle to do so authoritatively without direct human input. Filling all the ReRafts (see later section) with the necessary details for an overall efficient virus-defense that has a solid basis in experimental knowledge requires a myriad of small tasks to be done. That is where *wid-e* research is a much stronger candidate for doing this well than much university research.

The purpose of this study is to test in simulations, whether the amount of change in transmission probabilities required for stopping the virus is in an order of magnitude that might be achievable by an ad-hoc crew of people who are just getting started with the whole idea. While that might indeed be the case, there is also the point of general pandemic safety, which means that even if we can't do enough of it now to stop this virus, there is no better time for starting with the necessary training than right now in the middle of this pandemic; who knows, maybe we can stop a substantial part of this one still.

9. What sank the Titanic? Lessons for World War V

9.1 Do we need the precise location of each iceberg before slowing down?

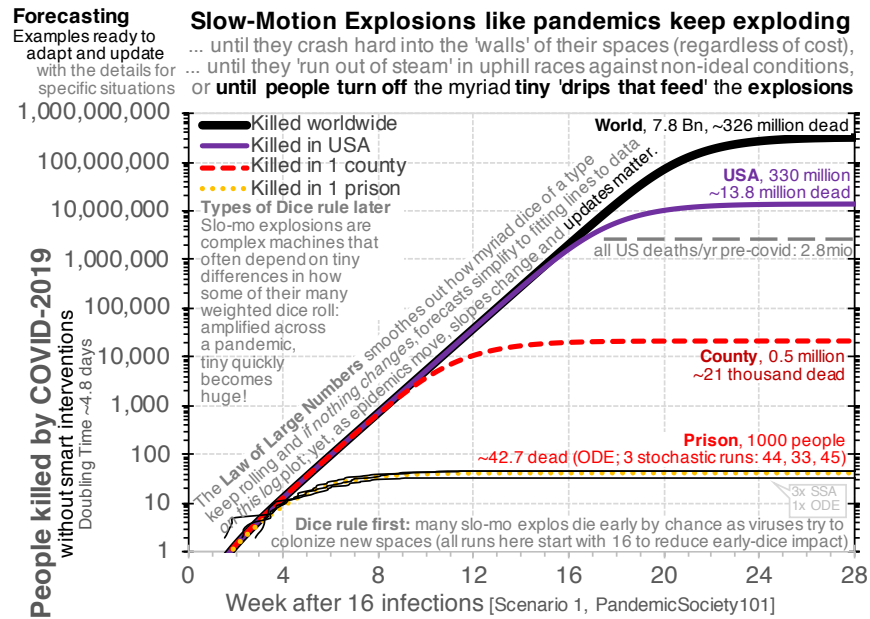


Fig.9-1: Overview of potential consequences of 'simply going back to normal' and 'forgetting about the Coronavirus'. This perspective on different scales is one of many in the set of biologically reasonable scenarios and by far not the worst one that could have been picked. Countries lucky enough to reign in the virus within their own borders need to consider that it requires world-wide victory to win in WWV, or else the arrival of ~16 new infections can start a new cycle with a new variant that will have evolved into an unknown direction. Thus, the virus tests willingness to help others in distress, equality of human dignity, and social cohesion as much at the international level between nations as it does for individuals within nations. Rough comparisons to other death rates or events: assuming globally ~17.9 million/year die of Cardio-Vascular Disease (CVD), USA ~647,000 /yr CVD, means CVD the biggest killer disease takes ~18 or ~21 years to kill as much as this wave easily can if not fought. For the USA, assuming flu kills ~46,000/yr makes COVID-19 ca ~300-fold deadlier; if 'Little Boy' killed ~120,000 in Hiroshima, this Coronavirus wave drops the equivalent of ~115 Hiroshima bombs on the US unless stopped intelligently as discussed. Such death rates are hard to estimate, so margins of error likely exceed *1/2 on a log-scale – instructive to compare to those killed in the 9/11 attacks.

9.2 When will we start to protect the most vulnerable first?

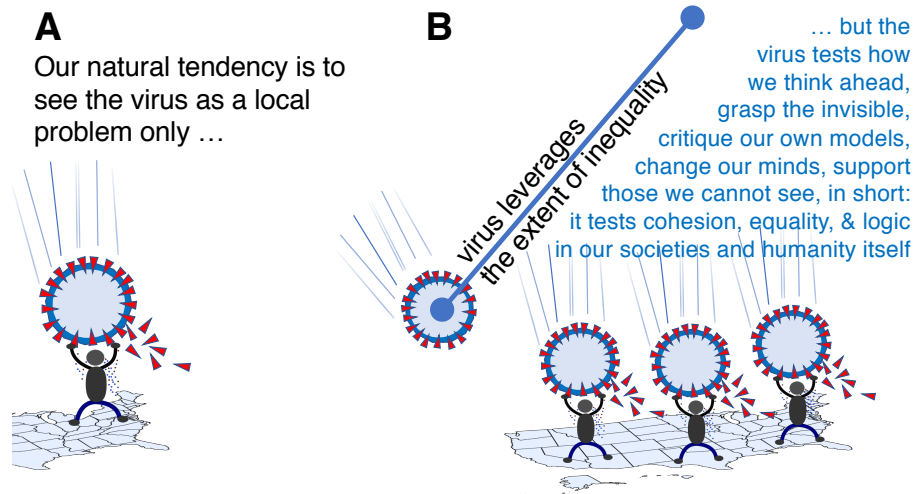


Fig.9-2: Analogy of the Coronavirus Millstone Mountains, aiming to illustrate for our linear world what happens in the multiplicative world of the Coronavirus. **(A)** Dealing with the virus assault would be bad enough as it is if all burdens were shouldered equally. **(B)** Inequalities make it worse: when essential workers in health care and elsewhere are exposed to more risk, the virus can damage valuable common infrastructure and training investments and then do even more damage {National Center for Health Workforce Analysis, 2014 #29041;Gould, 2020-06-01 #29042;Wurth, 2020-06-29 #29043}. The same is true internationally {Wintour, 2020-07-16 #29044}. History suggests that in such cases, the worst cases should not be discounted too fast: cheap decks of the Titanic were filled with water before the expensive ones, but all sank; a severe self-induced shortage of doctors and a logic based on inequality led to surprisingly preventable deaths {Iannuci, 2017 #28502;Wilde, 2018-12-24 #28503}; John of Ephesus remarked about the so-called First Pandemic in 542 C.E. that it was kind to the poor, because they died first, at a time when there were still people around to bury them. The Coronavirus is by far not the worst problem with the strong potential for such a dynamic. If our civilization cannot defend Earth against this we may force ourselves into having to repeat a good part history we would have hoped we learned.

Our minds are primed on intuitively grasping the linear calculus of Newton, because we all grow up in a world, where time, space and mass behave in ways that are extremely well approximated by a linear calculus. Our intuitions know it, even if we struggle with Newton's equations. However, the Coronavirus pandemic does not live in a linear world and thus does not follow Newton's laws. Instead, it follows the calculus of slow-motion explosions, that is difficult for us to grasp intuitively, even for those who have learned a few of the relevant equations. Learning the equations is not the point here, but grasping the intuition is. **Fig.9-2A** attempts to translate what is happening in the non-linear world of the coronavirus back into a scenario that our intuitions can (maybe) handle a bit better. Imagine, the coronavirus was a millstone from space, had the size of a few mountains and was about to smash into a nation unless it stood up like a determined warrior and defended itself by pushing that huge millstone back into space. Imagine it could actually do that (as the results of this study suggest), clearly requiring an enormous effort, even in the best of cases. That is depicted on the left. **Fig.9-2B** Complications from inequality are like additional lateral forces that can easily throw off-balance. Since the virus does

not follow a linear calculus, it attacks in many ways. It first hits those most vulnerable (often the poor) and then works its way up to those who depend increasingly on the services of others. Eventually, the repercussions even reach the last of those who have the best security money can buy. Yet, by the time their linear intuition gets through the noise of glitzy preoccupations to warn them, their ability to contribute to reparations of virus-defenses where it matters most will have shrunk dramatically. Rephrased in terms of the Titanic story: as long as the breach of the ship is a problem for those with the cheap tickets, it's a problem for everyone.

9.4 How long will we wait before completing the four freedoms from WWII with its most profound discovery, the Freedom of Research?

9.5 Chance, necessity, and self-fulfilling prophecies:
About metaphysical belief systems in this pandemic

9.6 The cost of doing nothing – interpreted by Arkhipov

10. Conclusions

Acknowledgements

Supporting Information

Figures + Sections omitted; see ToC below.

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Caring creativity: why *wid-e* research is a good investment

Draft: WWV training bootcamp for virus-defense and modeling

SO: Table of Content (roughly)**1. Introduction****2. Modeling and Evolvix: a micro introduction**

- 2.1 High-quality models as maps to reality: useful *because predictably* wrong
- 2.2 Reality and its views from different mapping styles, modeling techniques and frameworks – why these matters
- 2.3 Example: A pure mass-action modeling framework implemented by a prototype for the Evolvix language aim to simplify accurate modeling
- 2.4 Integrating knowledge-uncertainty from different realms in biology
- 2.5 Logics, the witches of andOr, and virus-safety
- 2.6. The Evolvix Mission, Vision, and wide interdisciplinary diversity-encouraging (*wid-e*) research

3 Pandemics challenges to EvoSysBio, current research culture, and beyond

- 3.1 The Coronavirus as a grand research challenge for EvoSysBio
- 3.2 Mathematical challenges from Coronavirus EvoSysBio
- 3.3 Biodata Science challenges from Coronavirus EvoSysBio
- 3.4 The importance of *wid-e* research for finding integrated solutions

4 Mission Impossible: Timers to stop a slow-motion explosion

- 4.1 HalfMax clock: a rough timer for the brunt of a slow-motion explosion
- 4.2 LastFive clock: a rough timer for defusing a slow-motion explosion
Show what to enter in R + simple equations for pocket calculators
- 4.3 Comparisons to observations in the US up to May 2020

5 PandemicSociety101: an advanced SIR model that is more realistic

- 5.1 Overview of the PandemicSociety101 model for the Evolvix prototype
- 5.2 Comparison of PandemicSociety101 to typical SIR models
- 5.3 Aggregated State Homogeneity Approximators of well-mixed populations
- 5.4 Functional extensions of the PandemicSociety101 model and observations about the efficiency of programming language paradigms
- 5.5 Overview of ‘back to normal’ Scenario 1 in PandemicSociety101
 - 5.5.1 Choosing values for the Input Parameter Use Table: Scenario 1 InPUT
 - 5.5.2 Deterministic (ODE) and Stochastic (SSA) OutPUT for Scenario 1
 - 5.5.3 Overview of the core OutPUT for Scenario 1 PandemicSociety101
 - 5.5.4 Why the simple SloMoExplo timers are surprisingly useful
 - 5.5.5 Pragmatic approach taken to InPUT for Scenario 1

6 Pandemic Death Traps to watch out for

- 6.1 Expecting death to follow simple rules
 - 6.1.1 Why are mortality rates so complicated? – decision-making & learning
 - 6.1.2 PandemicSociety101: Mortality rates when ‘everything’ is known.
 - 6.1.3 How DoR DoC mortality rates might vary across states in the USA
 - 6.1.4 How DoR DoC mortality rates might vary internationally
 - 6.1.5 Surprising problems with mortality rates
 - 6.1.6 Why mortality rates matter less and matter more than some think
 - 6.1.7 Cassandra’s regret and disinterested scientific predictions
 - 6.1.8 Pragmatic approach taken in this study
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- 7.8 How to stop this pandemic? – How to make the rules?
- 7.9 How to stop this pandemic? – Taking World War V seriously, but how?
 - Fig.7-6 WWV lines of defense
 - Fig.7-7 Overall integration of epiEYEkeia strategy in 1 HD map
 - Who is the enemy?
 - Who is not the enemy?
 - Fig.7-8 Ethical compass
 - Point to appendix for more details

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