Normal science and the hidden lemmas of mathematical epidemiology *

Mathematical modeling COVID-19

Hernán G Solari[1] and Mario A Natiello[2]

[1]Departamento de Física, FCEN-Universidad de Buenos Aires and IFIBA-CONICET, Argentina
[2]Centre for Mathematical Sciences, Lund University

October 21st, 2020

Abstract

Normal science is a characterization of science in our epoch and a demarcation of what "scientific" means. It divides science in disciplined/normed paradigms. Mathematical epidemiology is the paradigm that regulates the activity of mathematicians with respect to the study of epidemics. It also represents the interest (multiple meanings implied) of the community that guards it. In contrast, a real epidemic is a complex system, an undisciplined problem. To enable a connection between reality and the paradigm, an important number of bold decisions are needed: the hidden lemmas, i.e., simplifying assumptions that are not offered to examination and are usually inscribed in the habits of the practitioners of the paradigm. The right of mathematical epidemiology to speak about real epidemics rests on the appropriateness of the reduction of the problem to a schematic set of equations or algorithms. We offer an examination of the most evident hidden lemmas in action.

Keywords: philosophy, modeling, biology
Mathematical Subjet Classification 2010: 00, 92

1 Introduction

What we call science has taken different forms in different epochs, evolving with the transformations of society. Several periods can be distinguished. Let us start with an early period in which the goal was to seek the harmony of the universe.

*To appear in **MATHEMATICS FOR HUMAN FLOURISHING IN THE TIME OF COVID-19 AND POST COVID-19** DeGruyter Proceedings, ISBN 978-3-11-073862-9

Natural science was known as Natural Philosophy and the people involved in it, more often than not, called themselves "Philosopher and mathematician" as for example did Galileo, Descartes, Leibniz and Newton. The period ended around the middle XIX-century when "in one generation", as Ortega y Gasset (1930) puts it, the wise men disappeared, their place being occupied by the specialists. The sciences were separated from the body of philosophy and from the strict controls of reasonability. Every discipline would set its own rules, its norms, which the scientist should follow, for otherwise they would not be recognized as members of the discipline. Mathematicians no longer had to account for the reasonability of their hypotheses (that became axioms) as long as they were consistent (this issue is not trivial as well (Wagon, 1985)).

Physics would be good as long as it were able to predict (see for example (Einstein, 1940; Popper, 1959)). Biology, medicine and all the professions and sciences followed their own rules and the unity of science and reason became broken. Out of the second industrial revolution a new social role for science emerged: science would nurture the development of technology and mankind, instead of understanding nature, was set forth to dominate nature.

After the successful involvement of science in the so-called World War II (1939-1945) the mandate for science to be the engine of the economy took force (Solari *et al.* , 2016). Science was professionalized, thus taken the opposite attitude of philosophy according to Kant (1798), and for such effect it was further disciplined and subdivided in specialized (self-referencing) communities or paradigmatic groups. *Normal science* (Kuhn, 1962) was born.

The integrity of science, and then science itself, was further damaged by dividing disciplines into a "pure" and an "applied" part. While the "pure" discipline would dedicate its efforts to speculation, the applied part was to use the results of speculative thinking in the solution of problems or the development of opportunities (Feibleman, 1961). Not only a hierarchy between both groups was established but the flow of questions and problems from the real (observable) world to the speculative group was interrupted. The applied group was charged with the duty of producing social value for the outcome of the pure group [1]. Nobody apparently remember that Gauss, the prince of mathematicians as he was often named, constructed the first telegraph, it connected his office in Göttingen with Weber's office, his friend and collaborator. Gauss was involved in developing Electromagnetism, which required some of the mathematics that he developed. Do we remember that Kant is considered the first geographer or that we have the Second Law of thermodynamics mostly thanks to the efforts of a french military engineer, Sadi Carnot, seeking to reduce the expenditure of scarce charcoal by steam engines?

Scientists became oriented by goals, ultimately set externally by the flows of money (Lucier, 2012) directed to facilitate their work (including a salary). In any system administered through goals, success (i.e., achieving the goal) becomes the most important part of the activity. But goals, if they are going

[1] Feibleman distinguishes Technology as a subset of Applied Science, further away from speculation and closer to practical problem solving. For the sake of this article there is no need to make this distinction.

to be measurable as it is needed for administrative purposes, need to be well-defined and achievable. For example, *understanding* is not a finite, achievable and verifiable goal; *predicting* as well as *developing new products* are possible goals for normal science. In the same form, for administrative purposes (say, for directing the flow of money) quality cannot be measured while quantity is a measure in itself. Thus, normal science accounts science by production, counting ”least publishable units” (LPU (Broad, 1981) or MCPU for “minimal content”) and socially related numbers such as the number of citations that illustrates how a MCPU has been involved in the production of new MCPU’s. With these changes, science became techno-science and is to be accounted for by the rules of technology, since success, achieving the goal, is what decides the value of a technology, being of no importance whether there is understanding involved or mere ”trial and error”.

As a consequence of its new social role and accounting, normal science proceeds by small increments extending the established paradigms; it seeks opportunities of application of already accepted knowledge (Traweek, 1992). Consequently, it is not well prepared to deal with new phenomena, such as for example the COVID-19 pandemic. Instead of trying to understand the problem ”in itself” it will try to fit it in its predefined boxes. Ortega y Gasset (1930) dictum must be recalled ’The specialist “knows” very well his own tiny corner of the universe; he is radically ignorant of all the rest [...] We shall have to say that he is a learned ignoramus, which is a very serious matter, as it implies that he is a person who is ignorant, not in the fashion of the ignorant man, but with the petulance of one who is learned in his own special line.’

For a phenomenon as the COVID-19 pandemics that involves biology at different levels (population dynamics, population genetics, virology, immunology and medical issues), sociology and social-psychology as well as politics, the task of reducing it to ”mathematical epidemiology” appears to be possible, at this early stage, only by a complete misrepresentation of the phenomena.

Before discussing the hidden lemmas of Mathematical Epidemiology, let us discuss how the old science worked in front of phenomena (meaning not only the fact but the extraordinary as well). Figure 1 illustrates the cycle. We begin by the observable, be it directly or through experiments. The map Π, called the *phenomenological map*, represents two steps: The first step is the philosophical ideation (Husserl, 1983) which consists in the action of the intuition supervised by reason to produce an idea out of the observed, it is this idea what we call *fact* (Piaget & García, 1989). In our case, the process continues by writing down the idea in mathematical terms. The map Π is a projection as it strips the observed of several features that are judged to be irrelevant for the matters under consideration. This is to say that the ideation is not independent of the questions we want to address, or what is the same, the model is not a copy of the phenomena in mathematical terms. The lift Γ represents the inverse process in which the ideated is reconstructed as observable reincorporating the stripped elements. The relations $\Pi \circ \Gamma = Id$ and $\Gamma \circ \Pi = Id'$ are needed if we are not to introduce distortions in interpreting results. There is no ”free interpretation of results”. Finally ϕ is the mathematical and logical elaboration of the theory.

The half cycle $\Gamma \circ \phi \circ \Pi$ produces expectations of new observations that allow us to check the theory. In case the check fails, the same cycle run in inverse mode (red arrow in Fig. 1) will indicate points where our original ideation was incorrect and need to be changed. Learning is the event in which we change our ideation, changing facts associated to the observed. The cycle of learning is continuously running and we are continuously learning, i.e., replacing a theory (useful belief) by a new one that we choose only because it is more appropriate for the fundamental task of organizing the observed phenomena. The process is called abduction (Peirce, 1955; Burks, 1946) and the present version is inspired in García (2006).

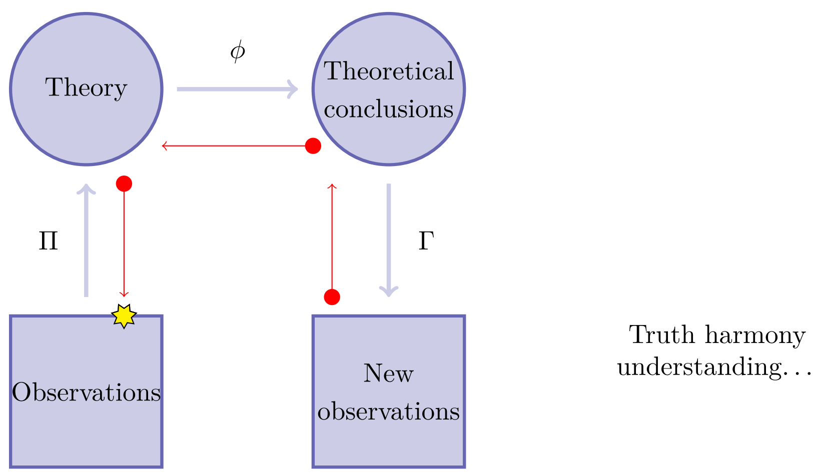

Figure 1: A cycle in the creation of understanding.

In contrast, normal science can be schematized as in Figure 2

2 Epidemics are complex systems

There are several, contending, definitions of *complex systems* and we will adhere to none of them although we will be close to that of García (2006) and actually develop it from the seminal discussion in García (1981).

The characteristics of a complex system are: the system exists in nature and interpellates society as a whole (not just the practitioners of a discipline). As a system, it is composed by several subsystems in reciprocal influence, and the functioning of a subsystem within the system cannot be understood in isolation. Its study cannot be performed within a discipline or by the additive contributions of disciplines, it requires interdisciplinarity.

In summary: complex systems constitute complex problems that challenge the organization of normal science where problems are instituted and delimited by the paradigms (Bourdieu, 1999) and are solved within them, being their relevance only visible to the scientist trained in the paradigm.

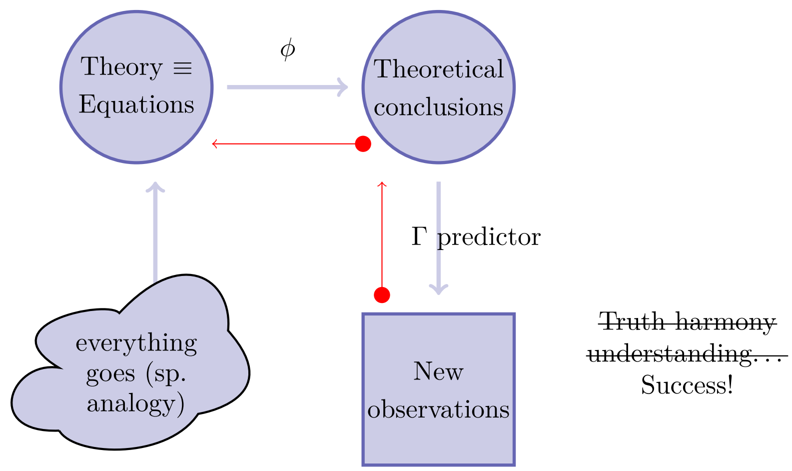

Figure 2: Scheme for normal science. (The expression ”Everything goes” refers to Feyerabend (1987)).

2.1 COVID-19 pandemic

Let us support our statement with the case of COVID-19 pandemic. The etiological agent is a ”new” virus (this is, a quasi-species) whose precise origin is currently being traced but almost certainly originates in wild animals (Shereen *et al.* , 2020; Hassani & Khan, 2020; Cazzolla Gatti, 2020) (at least bats act as *reservoirs*) and the pressure that human society is putting on wild species and their environments. Once the virus has minimally adapted to the vast environment offered by humans, the evolution process of the quasi-species accelerates thanks to the large number of replication opportunities that human population offers. Viruses constitute diverse populations that are permanently adapting and changing their identity, even more in the case of a RNA virus as SARS-Cov-2. To conceive them as fixed forms with fixed phenotypes is to run into a mistake. The genetic structure of the virus is continuously mutating, as well as the proportions of different genotypes in the population, since the quasi-species is continuously probing the environment and adapting, a process that implies the interplay of genotypes and environment (human beings in this case) (Hamilton, 2011) through an unknown function that determines the phenotype. Experience with other viruses indicate this function need not be ”smooth” with respect to the genotype, meaning that changes in a few genes may result in large changes in the phenotype (Minor, 2009; Morales *et al.* , 2009; Klitting *et al.* , 2018).

The immediate environment of the virus are the human cells, next the humans and through them society. Since we are mainly interested in the global view of the pandemic we will consider the level of cells only in terms of effects (rather than describing mechanisms). Hence, we will focus first at the human level. The human body will evidence the invasion by *symptoms* of various intensities and in the case of COVID-19 unspecific and often weak (China CDC, 2020; Chan &

Brownstein, 2020). The reaction of the human body to the invasion of foreign particles is effected by the immune system, which is complex in itself.

It has recently been found (Sekine *et al.* , 2020; Combes *et al.* , 2021; Mick *et al.* , 2020) that two different immune responses may lay behind the difference between mild and severe cases. Patients with mild COVID-19 exhibit a coordinated pattern of expression of interferon-stimulated genes (ISG), whereas these ISG-expressing cells are absent in patients with severe disease. The latter patients display a strong humoral response, higher levels of antibodies and lower viral load. Hence, mild cases could be more contagious than severe cases, not just because of differences in mobility and social contacts. The different responses may be related to age, sex and possibly other (unknown) factors.

Complexity triggers more complexity since different immune responses induce different selective pressures on the virus. Also, different severity of the disease influences contact networks and therefore the opportunities for virus spreading. The quasi-species population modifies its structure following reproductive success. Other social factors influence the evolution of the quasi-species as well. The decisions of society (mainly mediated by health authorities), such as isolation of high risk and infective cases, vaccination, etc., trigger different selective pressures on the virus as well.

2.2 Complex response to complex problems

Such a complex interplay demands a tailored response. There exists a genuine role for mathematics in handling complex problems, because of its ability to handle general structures, regardless of the supporting background. However, mathematics alone cannot get too far, since generalities and particularities are intertwined in complex systems. We will discuss in the next Section the paradigm of (normal) mathematical epidemiology, in order to identify its successes and shortcomings.

3 Mathematical epidemiology (the paradigm)

The basic ingredient in the mathematical description of an epidemic is a set of stages according to which the infection evolves in an individual, see Figure 3. The individual will evolve from a Susceptible state, S, to an Exposed, E, state after acquiring the illness, next to an Infective (or contagious) stage, I, finally ceasing to participate in the epidemic process at the Recovered stage, R.

Compartmental models will account for the number of members in each group (statistics a-priori) while individual based models will account for the stage of each considered individual (statistics a-posteriori).

The basic dynamics of the epidemic is then expressed as

$$\begin{aligned}\frac{dS}{dt} &= -\lambda_1 S \\ \frac{dE}{dt} &= \lambda_1 S - \lambda_2 E\end{aligned}$$

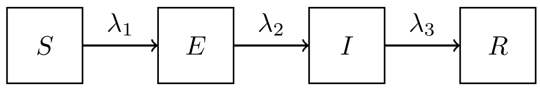

Figure 3: Basic stages in the evolution of an infection in a human being.

$$\begin{aligned}\frac{dI}{dt} &= \lambda_2 E - \lambda_3 I \\ \frac{dR}{dt} &= -\lambda_3 I \end{aligned} \qquad (1)$$

This approach goes back to (Verhulst, 1838).

To complete the picture, the rates λ_i are written in terms of the state variables (S, E, I, R).

The exploration of the paradigm begins in Equation 1, possibly modifying it through the inclusion of neglected elements (e.g., immigration effects, deaths, etc.). The main task of normal science is to expand the reach of the paradigm (Kuhn, 1962). Thus, normal science proceeds from a set of core beliefs (assumptions or "known" background) attempting to extend their frontiers of application. In contrast, the complex systems approach begins by becoming familiar with the problem, searching from there the mathematical forms that can better represent it.

There is a fundamental hiatus that goes from the concepts represented by Figure 3 and Eq. (1). It indicates the absence of a critical analysis of the phenomenological map Π. In the next section, we will address what are the demands of the phenomenological map, and hence what is assumed to be true when we follow the standard presentation of mathematical epidemiology, in the form of *hidden lemmas*, i.e., lemmas that are implicitly assumed as proved when we write the equations.

4 Hidden Lemmas

We shall divide the hidden lemmas by groups: mathematical, biological and epistemic.

4.1 Mathematical hidden lemmas

Populations are counted with integers, it can even be argued that integers were invented to count populations. An integer-valued function of time cannot be made continuous, and much less differentiable, except when it is constant. Hence the variables in Eq. (1) do not refer to the populations directly and some form of smoothing is needed.

There is a stochastic form of the process in which continuity corresponds to probability distributions, $P(S, E, I, R; t)$ that vary continuously in time following Kolmogoroff (1931) forward (or backward) equations, for systems that evolve with infrequent events of finite size ("jump" process). Feller (1940), showed that such process was associated with a generalized Poisson stochastic process (Durrett, 2001). Several results were obtained along these lines in mathematical epidemiology. Let us recall, because of its relevance, the concept of *critical community size* (Bartlett, 1957, 1960), which separates qualitatively different epidemic outbreaks. Additionally, below this critical community size the use of ODE's is completely meaningless, see Bartlett (1964) and others (such as Nåsell (1996, 1999, 2001); Aparicio *et al.* (2012)).

A series of works by T.G. Kurtz (Kurtz, 1970, 1971, 1976, 1978, 1981) discussed in (Ethier & Kurtz, 1986) unraveled the relation between the stochastic description and Eq. 1 as a large population limit of stochastic processes.

While in stochastic jump processes there is room for ”trapping” states such as those that result from the extinction of the disease, $I = 0$, the ODE replacement makes of these states an invariant set, i.e., either the solution belongs to such set for all times or it never reaches it. Extinction is therefore impossible. The limit process requires that the described states are such that $\lim_{N\to\infty} \frac{X_i(t)}{N} = x_i(t)$ for any population X_i, thus, any bounded population $X_i(t)$ is mapped to 0. The problem of extinctions cannot be fixed, it only indicates the limits of validity of the approximation.

Thus, in support of Eq. (1) we need to prove:

Lemma 1. Statistical requirements

a **Large population limit** *Eq. (1) represents the evolution of ensemble average values and its limit of valid use is given by a subsidiary set of equations (to be provided).*

b **Averages are representative of distributions** *The distributions* $P(S, E, I, R; t)$ *are sharply peaked around their average values.*

c **Exponential waiting time distribution** *The distribution of the times spent in each stage is exponentially distributed.*

Comment: Even when the process described in Figure 3 is implemented in terms of stochastic processes, the scheme requires to be complemented with a form of simulating the distribution of times spent in each stage and the variation of contagiousness along time.

4.2 Biological and social hidden lemmas

There are several facts assumed without saying in the basic model of Equation 1.

Lemma 2. Unstated biological and social assumptions

a **The virus does not change** *The phenotype of a virus does not change during the epidemic*

b **Contagiousness is independent of the evolution of the disease while the individual is infective** *Additionally, all individuals in class* I *contribute equally to contagion.*

c **Individual differences are irrelevant** *Human beings are immunologically identical and display a uniform response.*

d **Health policy interventions are represented by changes in parameters** *Control measures do not affect the core model. Instead, they are represented by adjusting numerical constants involved in the parameters λ_i.*

e **Social structure is largely irrelevant** *The sub-populations S, I, etc., represent the aggregation of average individuals. As a consequence, each individual in S, I, etc., is assumed to interact with any other individual without restrictions. Specifically, any I may transmit the illness to any S.*

Comment: Most remarkably, Lemmas 1a and 2e contradict each other within the framework of Eq. (1). Indeed, the underlying population should be sufficiently large so that the ensemble averages make sense, and at the same time sufficiently small so that uniform mixing becomes a realistic assumption. There exist no prescriptions for the scales of these processes but it is highly unlikely in general that they share a common region. Homogeneous mixing of human beings is impracticable above a few thousand individuals, while e.g., critical community sizes require hundreds of thousands.

4.3 Epistemic lemmas

Lemma 3. Fitting lemma
After dividing a data set in two parts: training and testing, parameter values can be optimized/obtained by fitting the output of the model to the training subset, and the quality of the model can be ascertained by evaluating the deviation of the model with respect to the testing subset.

Comment: The method is a method for compensating errors, it produces ”effective parameters” that adjust the output of a (possibly) improper model to the observed values. It makes difficult, if not impossible, to falsify (Popper, 1959) the model. By misrepresenting the strength of the causative elements identified while it continues to neglect other elements, the method drives us towards misunderstanding which, in our context, leads to improper preparation and consequently increased mortality. The idea appears to be supported by the belief that ”success is all what matters”. Additionally, it assumes that the context provided by the data is universal, i.e., that one sample of the stochastic phenomena can convey the information needed to predict the outcome of all the samples. In particular, it assumes that the future is a variant of the past.

Lemma 4. Incremental improvement
The effects can be disaggregated in terms of the causes, thus causative factors can be investigated separately and eventually aggregated at the end.

Comment: The lemma means that we can investigate for example different heterogeneities such as age, social structure and biological factors one by one and we expect the conclusions of the individual studies to hold true when we incorporate all the factors at once. Mathematically it represents a sort of linearity and additivity between causes and effects.

5 Conclusions

Kant (1798) considered just two types of faculties: the higher and the lower. He wrote:

> It is clear that this division is made and this nomenclature adopted with reference to the government rather than the learned professions; for a faculty is considered higher only if its teachings –both as to their content and the way they are expounded to the public – interest the government itself, while the faculty whose function is only to look after the interests of science is called lower because it may use its own judgment about what it teaches. Now the government is interested primarily in means for securing the strongest and most lasting influence on the people, and the subjects which the higher faculties teach are just such means.

While the higher faculties were regulated in their teaching, the only regulation for the lower faculty was reason. After Vannevar Bush's vision of science as the engine of economic progress (Bush, 1945) and the consequently harnessing of it by the states, the faculty of science moved from the lower to the higher level. Consequently, it lost its freedom since not only reason regulated it. Normal science had been born, putting an end to modernity. A new cycle of specialization took place and our ability to further understand phenomena was thwarted by the increased compartmentalization and the restriction of reason to its instrumental component (Horkheimer, 1947).

In more restricted terms, what is at discussion is whether the paradigmatic model of Eq. 1 can reflect all types of epidemic outbreaks (possibly after tuning parameters or introducing minimalist improvements) or, on the contrary, different epidemics must be reflected in terms of different mathematical structures resulting from their conceptualization.

The second element at discussion is the perception of the ”average” as representative of the totality or, what is the same, to disregard the consequences of variability. This usually implies a conception of ”mean plus noise” where the information is in the average –that follows deterministic rules and as such is useful for our predictive goals–, while the noise is a nuisance that we must ignore and simply blurs our prediction.

Paradigms are not suitable to challenge themselves, therefore normal science proceeds smoothly within the paradigm, with infrequent paradigm shifts (Kuhn, 1962). What are paradigms good for? Precisely to control those situations where input and output are clearly demarcated, known and expected. It would be a waste of time to reinvent concrete any time a new bridge or building needs to be raised. Paradigms offer a safe, stable way to proceed. In any case, the responsibility for correct application lies always on the side of the user.

As mentioned above, there is a genuine role for mathematics in epidemiology, for several reasons. First, the ability of mathematics of dealing with general structures. Also for its fundamental and inflexible commitment to logical consistency. In Figure 1, mathematics is the guarantor of the map ϕ. Moreover, mathematics may be able to suggest a way out of conflicts in the phenomenological map. However, the signification of mathematical procedures rests always in the understanding of the problem, i.e., in the phenomenological map. Mathematics alone cannot replace it but it does help to detect its possible failures.

Acknowledgement

HGS thanks exchanges with his colleagues in the Network for the Modeling of Infectious Diseases, a part of the Network of Research in Translational Medicine, CONICET, Argentina.

Both authors thank friends and philosophers Alejandro Romero Fernández and Olimpia Lombardi for fruitful discussions.

HGS acknowledges funds from the University of Buenos Aires under grant # 20020100100734.

MAN acknowledges a grant from Kungliga Fysiografiska Sällskapet i Lund.

References

Aparicio, J P, Natiello, Mario, & Solari, H G. 2012. The Quasi-deterministic limit of population dynamics. *International Journal of Applied Mathematics and Statistics*, **26**(2), 30–45.

Bartlett, M S. 1957. Measles Periodicity and Community size. *J. R. Statist. Soc.* **A**, **120**, 48–60.

Bartlett, M S. 1960. The Critical Community Size for Measles in the United States. *J. R. Statist. Soc.*, **A 123**, 37–44.

Bartlett, M. S. 1964. The Relevance of Stochastic Models for Large-Scale Epidemiological Phenomena. *Applied Statistics*, **13**(1), 2–8.

Bourdieu, P. 1999. The Specificity of the Scientific Field and the Social Conditions of the Progress of Reason. *Chap. 3, pages 31–50 of:* Biagioli, M (ed), *The Science Studies Reader*. New York: Routledge. Translated from an original in French (1975) by Richard Nice.

Broad, William J. 1981. The Publishing Game: Getting More for Less. *Science*, **211**(4487), 1137–1139.

Burks, A W. 1946. Peirce's Theory of Abduction. *Philosophy of Science*, **1**, 301–306.

Bush, Vannevar. 1945 (July). *Science The Endless Frontier*. Office of Scientific Research and Development, USA.

Cazzolla Gatti, Roberto. 2020. The pangolin's revenge: SARS-CoV-2 did not emerge from a lab but from wildlife exploitation. *GAIA-Ecological Perspectives for Science and Society*, **29**(2), 79–82.

Chan, Andrew T, & Brownstein, John S. 2020. Putting the public back in public health—surveying symptoms of Covid-19. *New England Journal of Medicine*, **383**(7), e45.

China CDC. 2020. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19)-China, 2020. *Weekly Vital Surveillances*, **2**(8), 113–122. `https://app.box.com/s/rprp4m855podhoruusiz5531zbz9d2dh/file/641837859060`.

Combes, Alexis J., Courau, Tristan, Kuhn, Nicholas F., Hu, Kenneth H., Ray, Arja, Chen, William S., Chew, Nayvin W., Cleary, Simon J., Kushnoor, Divyashree, Reeder, Gabriella C., Shen, Alan, Tsui, Jessica, Hiam-Galvez, Kamir J., Muñoz-Sandoval, Priscila, Zhu, Wandi S., Lee, David S., Sun, Yang, You, Ran, Magnen, Mélia, Rodriguez, Lauren, Im, K. W., Serwas, Nina K., Leligdowicz, Aleksandra, Zamecnik, Colin R., Loudermilk, Rita P., Wilson, Michael R., Ye, Chun J., Fragiadakis, Gabriela K., Looney, Mark R., Chan, Vincent, Ward, Alyssa, Carrillo, Sidney, Cathy, Cai, Zhan, Jenny, Samad, Bushra, Chak, Suzanna, Ghale, Rajani, Giberson, Jeremy, Gonzalez, Ana, Jauregui, Alejandra, Lee, Deanna, Nguyen, Viet, Yee, Kimberly, Abe-Jones, Yumiko, Pierce, Logan, Prasad, Priya, Sinha, Pratik, Beagle, Alexander, Lea, Tasha, Esmalii, Armond, Sigman, Austin, Ortiz, Gabriel M., Raffel, Kattie, Jones, Chayse, Liu, Kathleen, Eckalbar, Walter, Matthay, Michael, Erle, David J., Woodruff, Prescott G., Langelier, Charles, Kangelaris, Kirsten, Hendrickson, Carolyn M., Calfee, Carolyn, Rao, Arjun Arkal, Krummel, Matthew F., & Consortium, The U. C. S. F. C. O. M. E. T. 2021. Global absence and targeting of protective immune states in severe COVID-19. *Nature*, **591**(7848), 124–130.

Durrett, R. 2001. *Essentials of Stochastic Processes*. New York: Springer Verlag.

Einstein, Albert. 1940. Considerations concerning the fundaments of theoretical physics. *Science*, **91**(2369), 487–492.

Ethier, S N, & Kurtz, T G. 1986. *Markov Processes*. New York: John Wiley and Sons.

Feibleman, James K. 1961. Pure Science, Applied Science, Technology, Engineering: An Attempt at Definitions. *Technology and Culture*, **2**(4), 305–317.

Feller, Willy. 1940. On the Integro-Differential Equations of Purely Discontinuous Markoff Processes. *Transactions of the American Mathematical Society*, **48**(3), 488–515.

Feyerabend, Paul. 1987. *Farewell to reason.* Verso.

García, Rolando. 1981. *Nature pleads not guilty.* IFIAS Publiction: Drought and Man, vol. I. Pergamonn Press.

García, Rolando. 2006. *Sistemas Complejos.* Barcelona, Spain: Gedisa. Conceptos, método y fundamentación epistemológica de la investigación interdisciplinaria.

Hamilton, Matthew. 2011. *Population genetics.* John Wiley & Sons.

Hassani, Asma, & Khan, Gulfaraz. 2020. Human-animal interaction and the emergence of SARS-CoV-2. *JMIR public health and surveillance*, **6**(4), e22117.

Horkheimer, Max. 1947. *Eclipse of Reason.* Oxford University Press.

Husserl, Edmund. 1983. *Ideas Pertaining to a Pure Phenomenology and to a Phenomenological f Philosophy. First book.* Martinus Nijhoff Publishers. Translator F. Kersten.

Kant, Immanuel. 1798. *The Conflict of the Faculties (The Contest of the Faculties).* Der Streit der Fakultäten. Hans Reiss, ed., Kant: Political Writings, 2d ed. (Cambridge: Cambridge University Press, 1991).

Klitting, Raphaëlle, Roth, Laura, Rey, Félix A, & de Lamballerie, Xavier. 2018. Molecular determinants of yellow fever virus pathogenicity in Syrian golden hamsters: one mutation away from virulence. *Emerging microbes & infections*, **7**(1), 1–18.

Kolmogoroff, A. 1931. Über die analytischen Methoden in der Wahrscheinlichkeitsrechnung. *Mathematische Annalen*, **104**, 415–458. 10.1007/BF01457949.

Kuhn, Thomas S. 1962. *The Structure of Scientific Revolutions.* University of Chicago press.

Kurtz, T G. 1970. Solutions of ordinary differential equations as limits of pure jump Markov processes. *J. Appl. Prob.*, **7**, 49–58.

Kurtz, T G. 1971. Limit theorems for sequences of jump processes approximating ordinary differential equations. *J. Appl. Prob.*, **8**, 344–356.

Kurtz, T. G. 1976. Limit theorems and diffusion approximations for density dependent Markov chains. *Math. Prog. Stud.*, **5**, 67.

Kurtz, T. G. 1978. Strong Approximation Theorems for Density Dependent Markov Chains. *Stochastic Processes and Applications*, **6**, 223.

Kurtz, T G. 1981. Approximation of discontinuous Processes by Continuous Processes. *In:* Arnold, L, & Lefever, R (eds), *Stochastic Nonlinear Systems in Physics, Chemistry, and Biology.* Berlin: Springer.

Lucier, Paul. 2012. The Origins of Pure and Applied Science in Gilded Age America. *Isis*, **103**(3), 527–536.

Mick, Eran, Kamm, Jack, Pisco, Angela Oliveira, Ratnasiri, Kalani, Babik, Jennifer M, Castañeda, Gloria, DeRisi, Joseph L, Detweiler, Angela M, Hao, Samantha L, Kangelaris, Kirsten N, *et al.* . 2020. Upper airway gene expression reveals suppressed immune responses to SARS-CoV-2 compared with other respiratory viruses. *Nature communications*, **11**(1), 1–7.

Minor, Philip. 2009. Vaccine-derived poliovirus (VDPV): impact on poliomyelitis eradication. *Vaccine*, **27**(20), 2649–2652.

Morales, Mónica, Ramírez, Miguel A, Cano, María J, Párraga, Mario, Castilla, Joaquín, Pérez-Ordoyo, Luis I, Torres, Juan M, & Bárcena, Juan. 2009. Genome comparison of a nonpathogenic myxoma virus field strain with its ancestor, the virulent Lausanne strain. *Journal of virology*, **83**(5), 2397–2403.

Nåsell, I. 1996. The Quasi-stationary Distribution of the Closed Endemic SIS Model. *Adv. Appl. Prob.*, **28**, 895–932.

Nåsell, I. 1999. On the time to extinction in recurrent epidemics. *J. R. Statist. Soc.*, **B 61**, 309–330.

Nåsell, I. 2001. Extinction and Quasi-stationarity in the Verhulst Logistic Model. *Journal of Theoretical Biology*, **211**, 11–27.

Ortega y Gasset, José. 1930. *The revolt of the masses.* W. W. Norton & Company (1992).

Peirce, Charles. 1955. *The Philosophical Writings of Peirce.* Dover Publications. Selected and edited by Justus Buchler.

Piaget, J, & García, R. 1989. *Psychogenesis and the History of Science.* New York: Columbia University Press.

Popper, Karl. 1959. *The Logic of Scientific Discovery.* London: Routledge. First edition 1934.

Sekine, Takuya, Perez-Potti, André, Rivera-Ballesteros, Olga, Strålin, Kristoffer, Gorin, Jean-Baptiste, Olsson, Annika, Llewellyn-Lacey, Sian, Kamal, Habiba, Bogdanovic, Gordana, Muschiol, Sandra, *et al.* . 2020. Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19. *Cell*, **183**(1), 158–168.

Shereen, Muhammad Adnan, Khan, Suliman, Kazmi, Abeer, Bashir, Nadia, & Siddique, Rabeea. 2020. COVID-19 infection: Emergence, transmission, and characteristics of human coronaviruses. *Journal of Advanced Research*, **24**, 91–98.

Solari, Hernán G, Romero, Alejandro, Natiello, Mario A, & Lombardi, Olimpia. 2016. La ciencia administrada. *Sociología y tecnociencia*, **2**(6).

Traweek, Sharon. 1992. *Beamtimes and Lifetimes.* Cambridge, Massachussets and London: Harvard University Press.

Verhulst, PF. 1838. Notice sur la loi que la population suit dans son accroissement. *Correspondance Mathématique et Physique*, **10**, 113–121.

Wagon, Stan. 1985. *The Banach-Tarski paradox.* Encyclopedia of Mathematics and its Applications. Cambridge University Press.