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SCIENCE DYNAMICS REVIEW®

JOURNAL FOR THE DEVELOPMENT OF SYSTEMS EDUCATION
ČASOPIS PRO ROZVOJ SYSTÉMOVÉ VZDĚLANOSTI

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V TOMTO ČÍSLE:

Science Dynamics Masterclass

Quod factum est, ipsum permanet; quae futura sunt iam fuerunt ...

Because there's nothing new under the sun and all things already were...

Once more for the thick-headed...

-aur-*

Abstract: Loose continuation of the article "Salvation, Ltd." from SDR No. 11, in which considerable attention is paid to viral mutations and its consequences. The second part of the article deals with a systems view on innovations in respiratory protection and the last, third part examines strategies and policies for dealing with mutating pathogens.

I am happy to announce that the proof of the existence of god, diligently sought from the beginning of times, **has finally been found**! It is completely out of the question that **someone else** would punish us with such politicians, officials and various servants and enforcers of secular justice ...

The best possible title of the introductory article of this issue seems to be the statement of my wonderful teacher of the Czech language, which I remember with love even after many years. The breathtaking optimism with which he repeated language rules over and over in the hope that at least one of the dull-staring creatures in the classroom would understand is an inspiration for similarly useless work I am doing right now... Even though so much time has passed since Jenik's untimely death caused by an insidious demyelinating disease.

Several readers wrote that they did not understand the conclusion of the article entitled "Limited liability salvation" from SDR No. 11 and still had no idea what should happen to grandma from bohemian city of Pardubice. I've found that creating a hint is not enough to some, because not only can't they read between the lines, but they don't want to try it either, saying that I should be thankful that someone reads my texts at all...

Not this way, friends! Even my beginner students know that lowering the bar is not a way to raise the masses, but is subject to the archetype of Erosion of goals, described in detail in the available literature [1]; for he who has once begun to back down will never take a step forward again. We, to whom the state of ignorance gives rise to nausea, will in the meantime seek answers to questions related to the current situation, divided into three parts (or topics), and whose absence contributes to the development of ignorance.

Part I. - Et nos mutamur ...

It is probably the result of an epidemic of **delusions of eternity**, which invaded mankind long before FauCo7 appeared, that makes them operate within the *carpe diem* strategy and remain indifferent to everything related to future things. It is easy to explain that the desperate search for constants was already evident in Archimedes' famous statement, who was ready to move the Earth from a fixed point. We can go even further into the past and recall Solomon's statement that although generations come and go, "*terra vero in aeternum stat.*" Well, Isaiah's prophecy was written several centuries after Solomon's death, so Solomon had no idea of the **temporary nature** of the Earth...

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* Editorial office: SDR@sciencedynamics.net

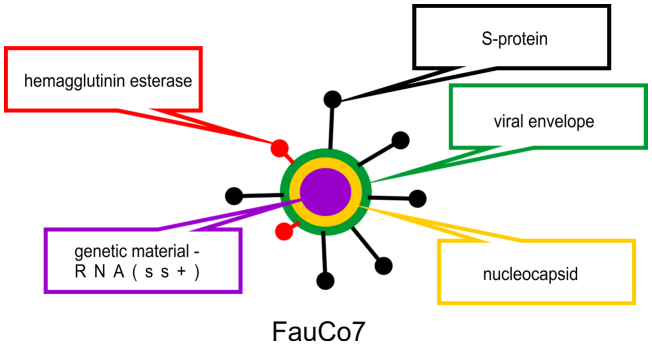

Fig. 1 Simplified FauCo7 virus structure

How such a mutation works and what mutations are the subject of passionate debates (especially in anarchist circles) in March of 2021 will be described in the following text. All of these processes form **feedback** in nature, but most of the links will be **left open** for training purposes and the completion of the diagrams will, as usual, be up to you. *Ecce* virus. I call it FauCo7 for myself, which probably is much closer to its true origin. The components of the virus important to our story are described in Figure 1. We already know from SDR 11 that FauCo7 uses its S-protein to mess with the infected organism. To make the description of the virus more complete, there's also viral envelope, nucleocapsid, hemagglutinin esterase and, of course, genetic material, in this case RNA ss+. The virus will, at least for now, be in its **original form**. The original form is definitely **not** the **wild type**, but let's keep the wild and tamed variants for one of our next meetings. Perhaps we will save a few words if you look at Figure 2 immediately after studying Figure 1, which simply describes the structure of the viral S-protein.

Our FauCo7 virus has a very strong affinity to **alveolar cells** (hence the respiratory problems of those infected). Simply put, the virus enters a cell by interacting with the cellular ACE-2 protein.

In addition, the process (receptor-mediated endocytosis) is **facilitated** by **transmembrane protease 2**, as shown under sequence number (1.) in Figure 3. When the virus is inside, its genetic material uses the cell's means of production to produce copies.

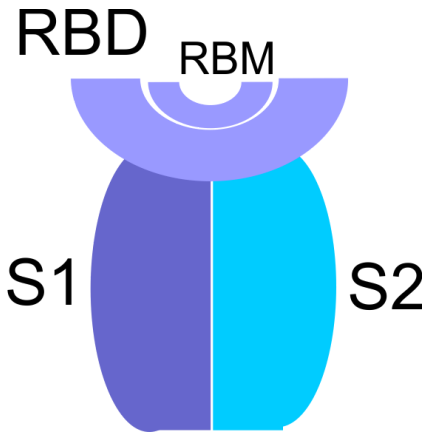

Fig. 2 Viral FauCo7 S-protein structure. S1, S2 and RBD (receptor-binding domain) are the main components of the protein. RBM is the contact site (receptor binding motif).

The detail of the RNA virus in Figure 4 indicates that one part of the genetic information (marked in black) encodes the S-protein, another part allows the production of **hemagglutinin esterase**, the next one codes building material for the **capsid**, in which the newly created virus will carry genetic information on its way to infecting another cell, the other parts then encode production of **RNA polymerase**, **replicase** and last but not least **protease**. From a simple RNA, the cell will make a pile of copies, the protease produces **polyproteins**, and the other components of the virus are formed, as shown in Figure 3 under the number (2.). All the material thus obtained is then packed in a neat package by Golgi complex (3.), which are subsequently (by fusion of the Golgi envelope with the cell membrane shipped out of the cell (4.).

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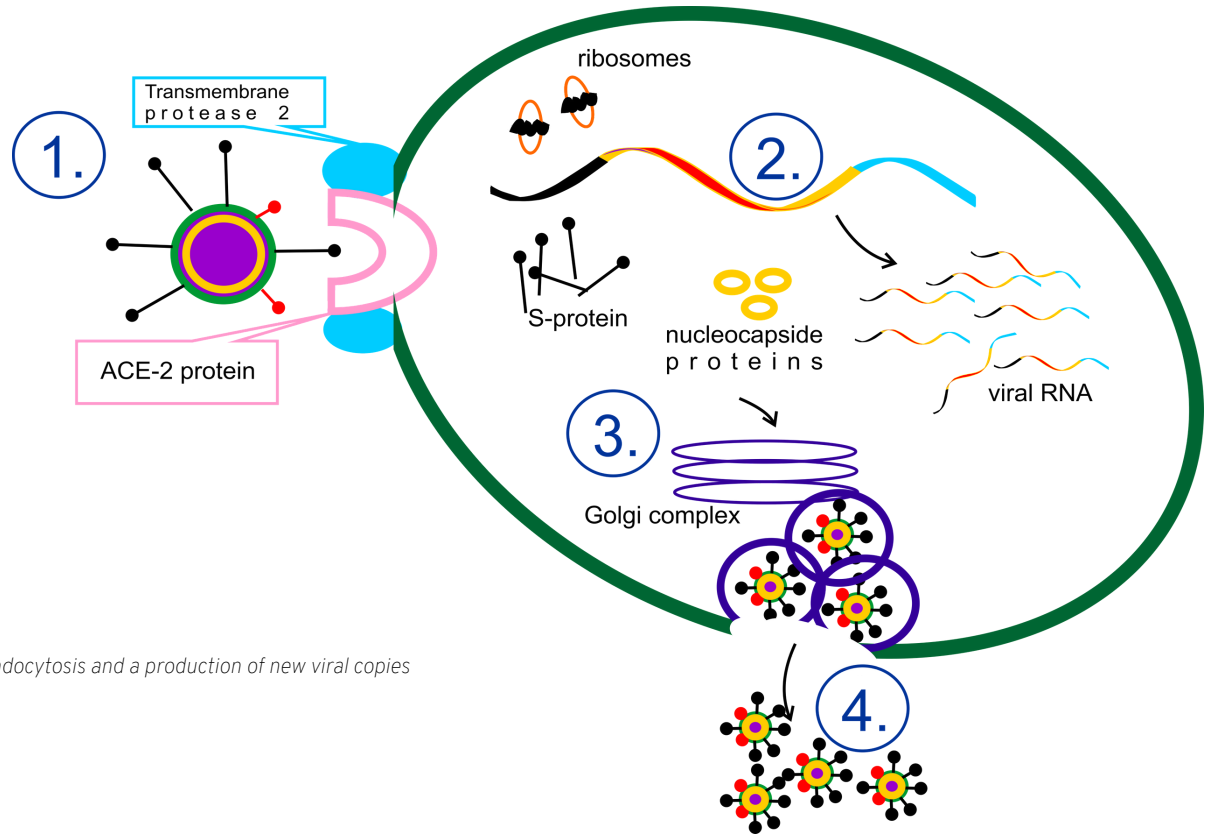

Fig. 3 Endocytosis and a production of new viral copies

The infected cell produces the virus copies until its death, often associated with depletion of the means of production and / or energy. The multiplied virus attacks other, so far healthy cells, blocks their original function and makes more copies. This goes on until the immune system deals with the infection or until the host is destroyed. *Omnia tempus habent et sui spacis*, which, in relation to FauCo7 and similar creatures, represents a diligent effort to improve theit chances of penetration into host cells, the **highest possible efficiency** in the production of new copies of oneself, and, if possible, without being detected or at least attacked by the host's immune system. You might even say: "How admirable behavior, the virus, in contrast with a certain part of the human population, actually **works hard** to earn its piece of pie, but you would be mistaken. That part of the population **is also working hard** on a way to parasitize more effectively on an ever-smaller herd of those who create real values.... continued on page 5 ...

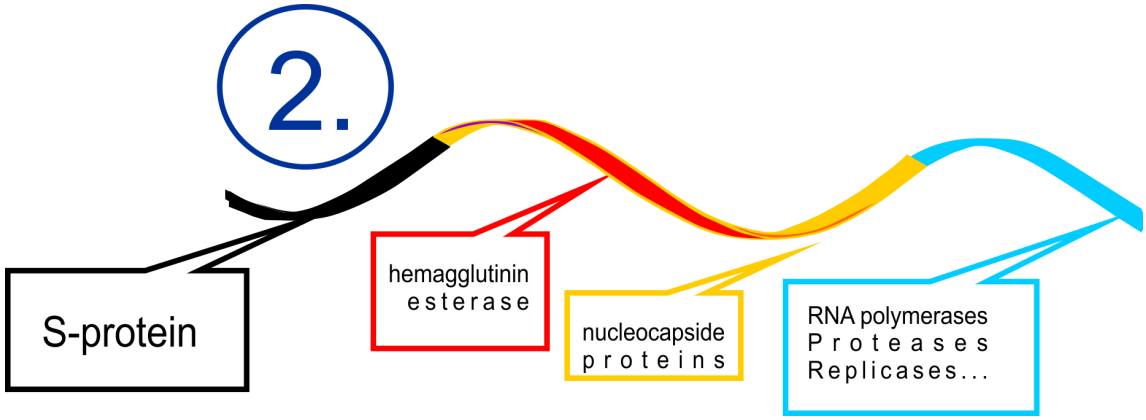

Fig. 4 Detail of the FauCo7 RNA

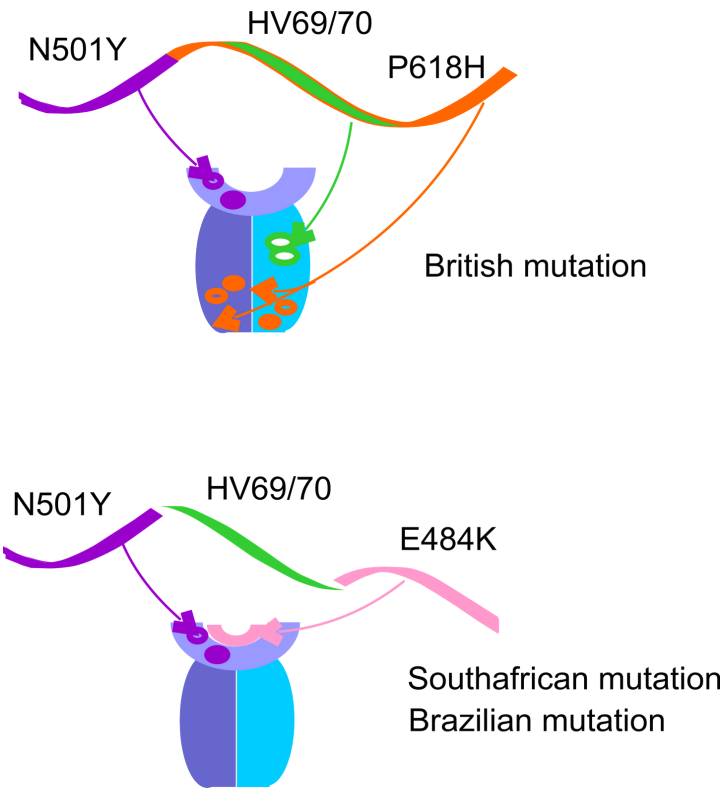

Fig. 5 Currently the most common mutations - British, Brazilian and Southafrican. Last two with mutated RBM - Receptor Binding Motif.

No one knows how many FauCo7 mutations are running around the world. We will stop at three of them and briefly describe them for the purposes of the third part of this article.

Figure 5 shows the currently most discussed mutations. Since these mutations involve all three major components of the viral S-protein, they are sufficient to explain the **most important consequences** of changes in the genetic code of the virus. For those who, unlike us, did not have to study Lewin's famous textbook [2] a short summary. The viral RNA sequence undergoes mutations over time. Mutations arise for various reasons, exo and endogenous, it is important that genetic code can be imagined as a sequence of instructions, based on which a new virus can be "knitted". When transcribing instructions from the "parent" virus to "children", sometimes a few instructions are lost, several of them are swapped between each other, in short, the resulting prescription, which wraps the Golgi complex in a package for shipment outside the cell, slightly differs from the original pattern.

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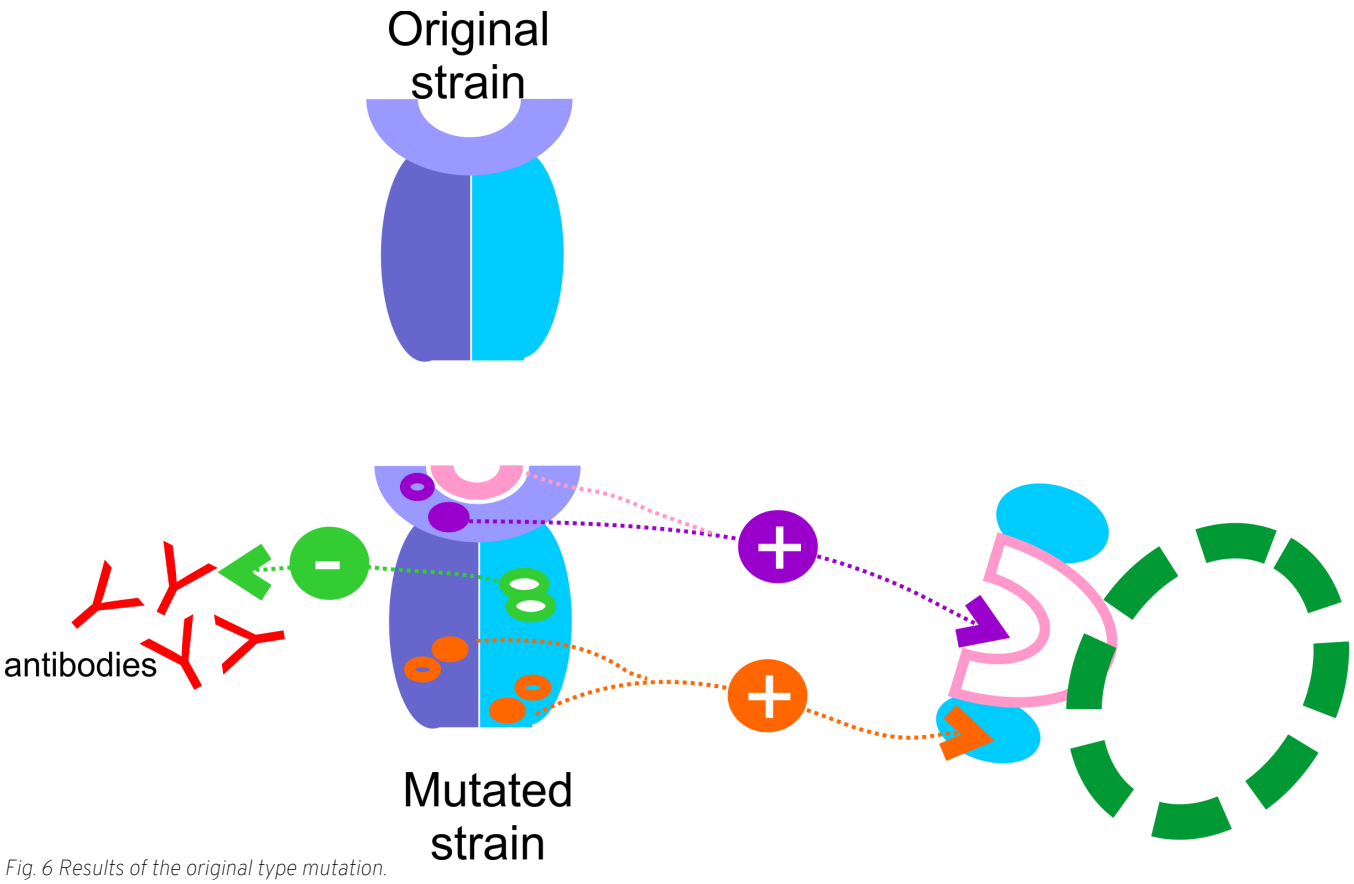
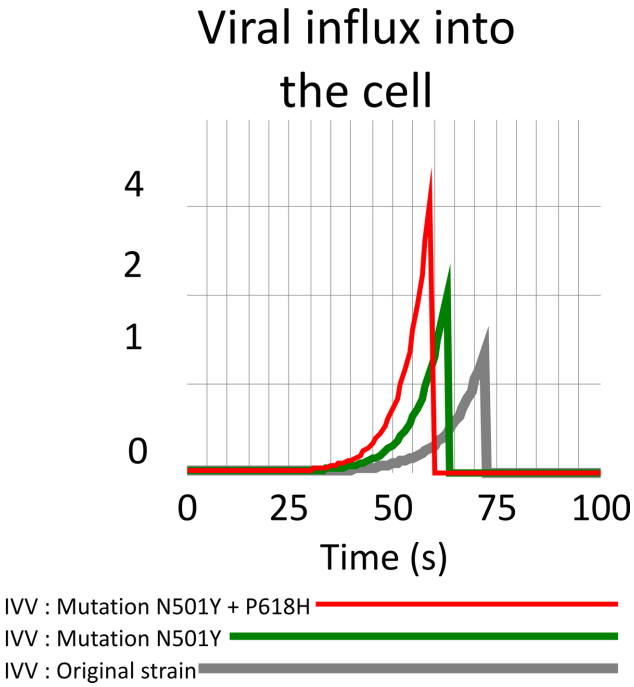


Fig. 6 Results of the original type mutation.

because the new sequence allows **easier penetration** into the cell, or **increases virulence**, or can better utilize the cell resources, but all above might apply at once. It is quite understandable that if a **highly virulent (infectious) variant emerges**, it will **spread far better** than a **less infectious sibling** and may eventually **become the most common variant in the world**. The so-called **British** or Kent **mutation** differs from the original pattern by **substitutions N501Y** and **P618H** and **deletion** on **HV69/70**. The Brazilian and South African variants also have the N501Y substitution, combined with the E484K substitution. Figure 6 shows what the individual mutations, cum grano salis, cause. In all of the above variants, the N501Y substitution increases the affinity of the RBD viral S-protein for the ACE-2 protein and thereby increases-facilitates virus entry into the cell, as indicated by the diagram in the figure with simulated behavior expressed in Graph 1. Note that the Y-axis is **exponential**. Explaining this phenomenon is not difficult, see Figure 7.



Graph 1 Viral influx index

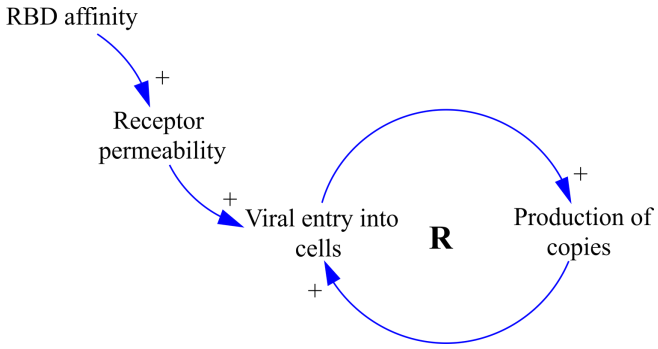
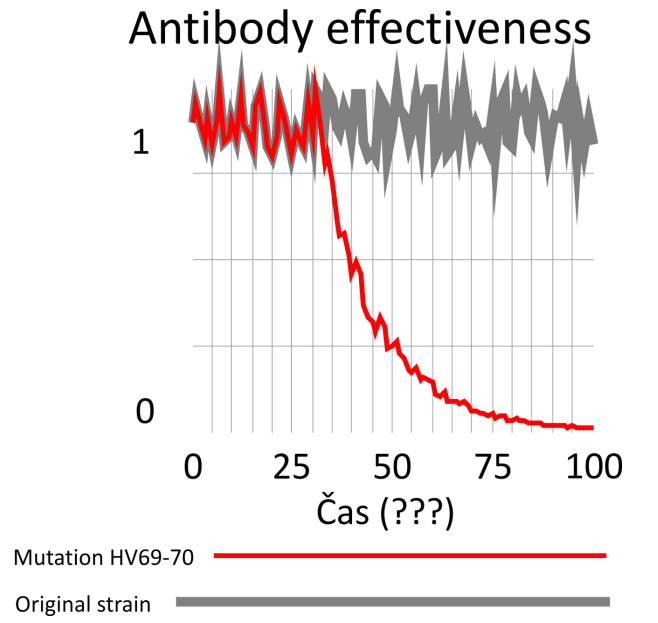


Fig. 7 The diagram shows positive feedback look in viral copies production.

In the British variant, the P618H substitution **increases** the **activity of transmembrane protease 2** and thus further **facilitates virus penetration into the cell**. Of course, a person with such an enhanced viral load is also more **infectious** than a person with the original variant of the virus.



Graph 2 Illustration of the impact of a mutation on the efficacy of antibodies to the original variant

The HV69/70 deletion induces changes in the **structure of the S2 component** of the S-protein, **reducing the effectiveness of antibodies** generated by both **infection** and **vaccination**, as indicated in Graph 2. Both graphs lack an accurate timeline description because reliable data are not available. The actual pattern can therefore (vertically) differ from the simulation.

..continued on page 7 ...

We have already described the N501Y mutation, also present in the South African and Brazilian variants, the E484K substitution altering the protein forming part of RBD that is in the closest contact with the ACE-2 protein and thus increasing / facilitating virus entry into the cell. The mutated component is called a **receptor binding motif** (RBM). These mutations increase their chances a little differently than the British variant, but they also do it successfully. It follows that mutations of the original virus are **significantly more contagious** and, in particular, **antibodies** produced after an illness caused by the original virus variant or a vaccine made from the original RNA **may not respond** to the British variant.

Part II. – What's that on your face?

The virus is still on the prowl and no light at the end of a tunnel is visible. After reading Part I, we are beginning to understand **why**. "Expert" teams all over the globe joined brains and came up with the idea: "If the virus thrives in the alveoli, why don't we order peasants to use more powerful means of **airway obstruction**, i.e. respirators, (*of course not*)preventing the entry or exit of viruses. Those who do not have respirator or cannot afford one, should make an űber-masks made of two, three or even more layers of material!" The reasoning behind multi-layer masks is **scientific**. If one layer provides 76% of protection, two layers give 93%, then three layers will get you to a very nice 110%! Let's be honest here. That is the level of protection our subjects **deserve**! Not sure what the UN is gonna do, but they might discover that having 110% of protection is one of, so far overlooked, **human rights**. Nitpicker will probably ask how it is possible that the degree of protection exceeds 100%, but we simpletons sense that the 10% is there to stay on a safe side and because such protection not only protects but probably also **heals**. If you feel that the above thinking should be treated by mental health professionals, you're right. The problem is that such and similar logic, as an epidemic, is already spreading in journals, which, in the past, bore the adjective "scientific." Therefore there is a study on the benefits-harmfulness of masks performed on an impressive sample of **four** (!!!!) participants. Other, substantially larger study, keeps kinda secret, that the design is **unable to distinguish** between "that" virus and its other alpha, beta, gamma, and delta strains, which have been with the mankind **since the beginning of time** and cause common seasonal respiratory problems. I will not intentionally state the source, according to the given data it is easy to find both articles. A terrible amount of similar treasures is coming out of the woodwork, and I do not intend to increase the value of these by citation, because the current horrible scientometry counts the **citation as a citation** and no matter the context. If I write that the author XY is a weak-minded creature, because the research he published is not research, but a pile of nonsense, the citation I made will be **included** in the number of citations of the article thus **increasing the article value**! If you shake your head in disbelief, that's probably the only thing you can do about it. In research, as we discussed in SDR number 10 [3], there is a problem with the experiment design. What question to ask and how to arrange it so that the experiment clearly answers the question asked and does not allow for an alternative interpretation?

... continued on page 8 ...

The tragedy of the scientist's situation is described in detail in SDR No. 7 [8], so it is not surprising that the design of experiments, if it makes sense at all, perhaps only appeals to the followers of the Gestalt, because it focuses on "here and now" and is interested neither in the initial context. nor in the future ***. In other words, forget that in the design of similar experiments, someone took into account the dynamics of the development of the investigated parameters. What do I mean? If a person is told to cough through a rag into a *Petri* (or *Pauli*) dish for ten minutes (for the benefit of humanity), every small child will argue that you need to measure effect right after deployment of the rag, then half an hour after deployment, two hours after deployment, and then six hours after deployment, because that's exactly how people wear their masks! But there is no such thing in the design. Why? Who knows. Maybe because something that we don't want to know could result from the experiment ... Figure 8 provides the basis of the diagram for creating an experimental design. It is therefore **not the result** of an experiment, but a **starting point**. Finish it to the final form as needed. The diagram describes the dynamics of conditions in the organism with the mask deployed in a way that does not occur in any of the studies found. Investigate the logic of a diagram with different combinations of values of exogenous variables (*Application time* and *Number of layers*) and design a meaningful experiment ****. For others, I remind you that it is possible to start a causal loop diagram from any variable, but I suggest you start from **exogenous** variables.

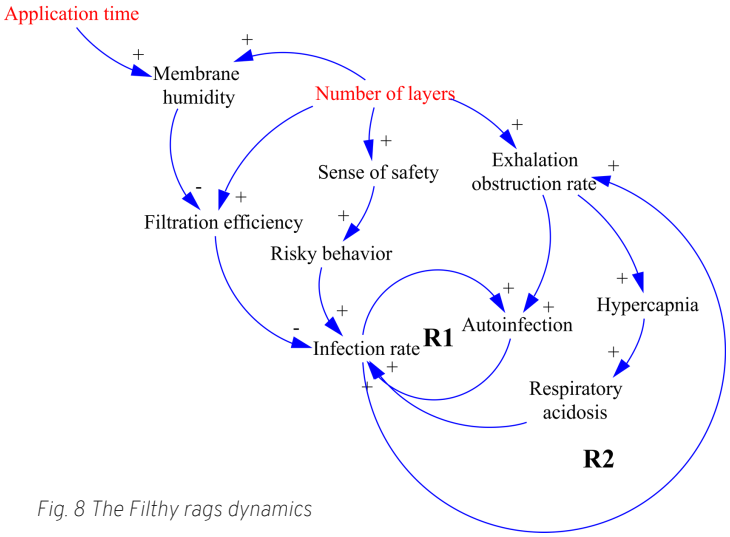


Fig. 8 The Filthy rags dynamics

E.g. The more **layers** (or product quality), the higher the **filtration efficiency**, but also the higher the sense of **safety**. The higher the sense of **safety**, the higher the probability of **risky behavior** (I am protected ...); the more **layers**, the higher and gradually increasing the **humidity** of the membrane and the lower the filtration efficiency ... You can playfully explore the rest of the diagram yourself. Then create a model according to the diagram and find out the actual course of *Filtration Efficiency* and *Infection Rate* over time. I'm already looking forward to your work. Both protective and diagnostic procedures will certainly evolve further. But maybe it won't be in the direction described above.

When I said, at the end of last year, to entertain the audience that a **rectal test** for the virus (of course significantly more sensitive and reliable than the current boogertest) will certainly appear soon, probably to increase the **self-confidence** of the already severely oppressed population, I had no idea that within a few a few months will become a reality ...

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*** Because the future always brings a good things...

**** For students: According to our pansophical evaluation model, the result will be included both in System Dynamics and in the Fundamentals of Scientific Work.

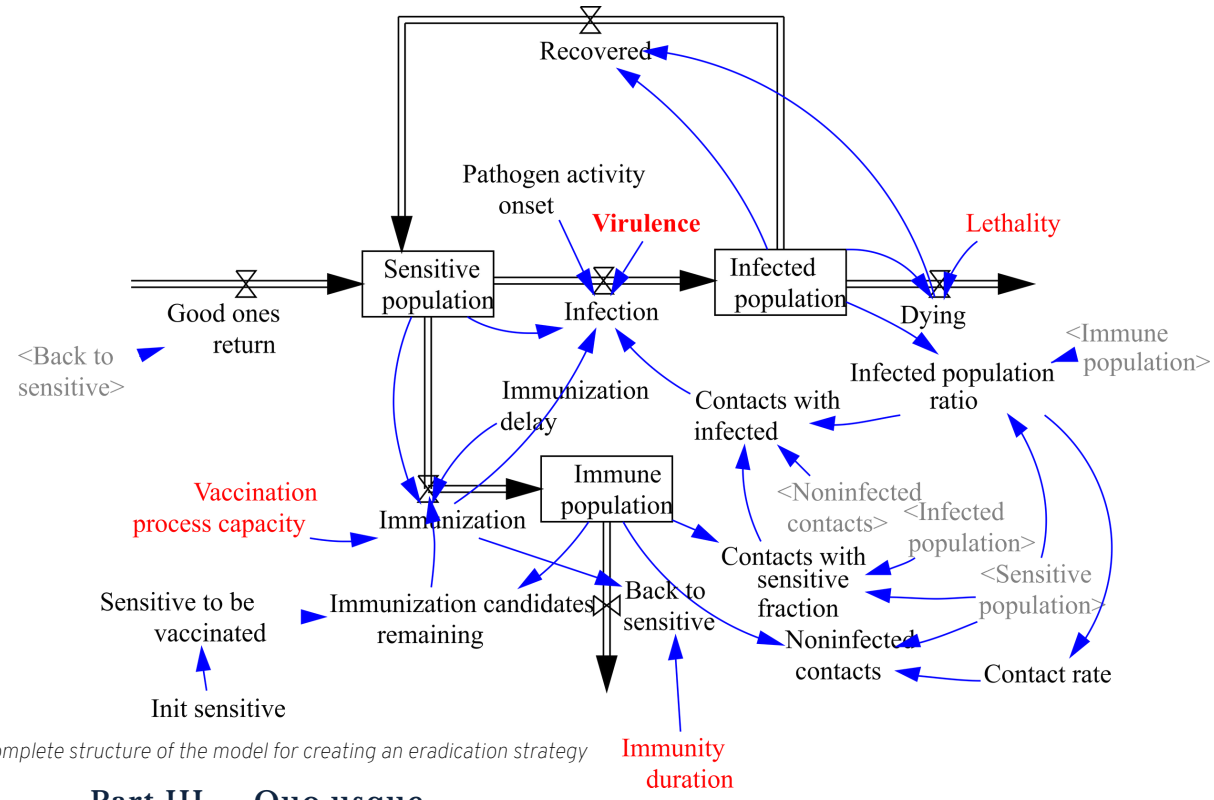

Fig. 9 Complete structure of the model for creating an eradication strategy

Part III. – Quo usque tandem abutere ... patientia nostra?

Scholars who know the introductory sentence of Mark Tuliu's most famous speech already suspect that the third and final part of this article will be devoted to simulating scenarios of further development based on the insight gained in the previous two parts. It is a tragedy that we published the structure of the model we will use in January 2020 [4] and described its main points in detail in the coming weeks and months [5-7], yet this had only a small effect on the meaningfulness of the target group's behavior. The complete structure of the model, which can be successfully used to create a functional **eradication strategy**, is shown in Figure 9. For completeness only, we published it with minor differences in June 2020 [7]. The model differs only in few features, vaccination is limited by the ability of the state to perform vaccination, lethality is now adjustable by slider, as well as the time for which the vaccinated population will be immune. We simulate one year with a simulation step of one day. Scenario S1 includes estimated virulence (infectivity) of the original form in the absence of post-infectious immunity and vaccine. We see that a system with a million people will get to steady state quickly. Sensitive people become infected to the extent given by *Virulence* and the *Contact rate*, some of them die depending on the *Lethality* setting, but others heal and return to being sensitive so that they can be infected again. Thus, the newly infected exchange beds with the healed, and the hospitals operate on the principle of **revolving doors**.

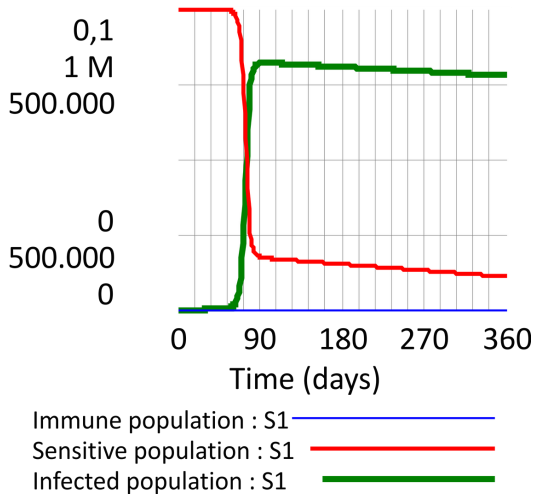

Fig. 10 Scenario S1 resulting in almost steady state

Figure 10 shows the result of the baseline scenario, in which the system is more or less in a steady state. The declining curves of the *Susceptible* and *Infected* populations are given by the fact that the model contains an outflow called *Dying*, but **not** an inflow called *Births* .... Scenario S2 in Figure 11 describes the policy in

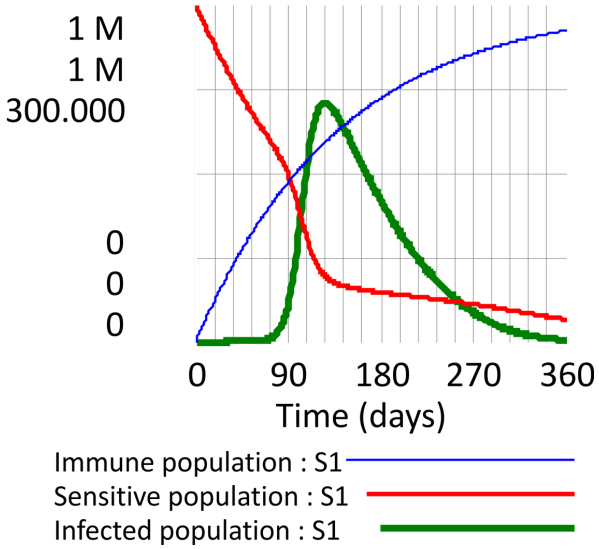

Fig. 11 Scenario S2 Successful eradication scenario

the same situation, but with a vaccine that manages, with an efficiency given by the constant *The capacity of the vaccination process,* to **inoculate a critical part of the population quickly enough**. The graph in Figure S2 shows the gradual disappearance of the *Infected*, a mere residue of *Susceptible* and a significant increase in the number of *Immune*. Scenario S3 describes the situation caused by the British virus mutation, where an even **more infectious** variant was added to the original strain and, in addition, the immunity to the **original variant** obtained by vaccination, described in detail in SDR 11 [9], is **temporary** and only **partially effective** against the new mutation. Nothing encouraging, is it? Nevertheless, the model can be used to find a successful policy that will lead to a scenario labeled S2 even in the presence of more infectious and the original antibody-resistant mutations.

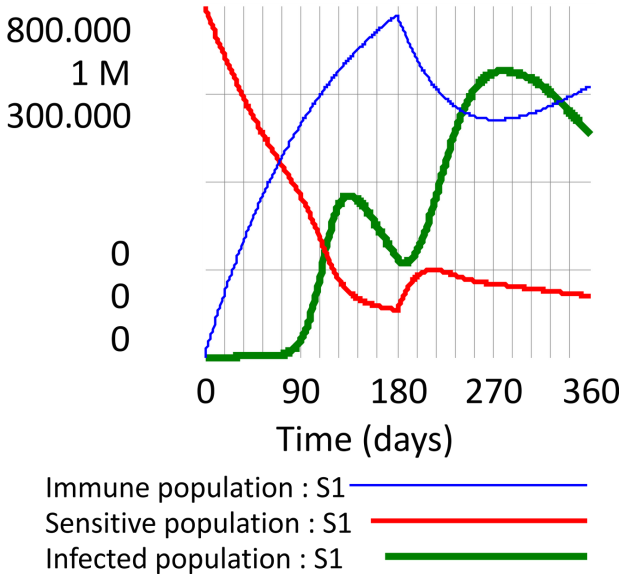

Fig. 12 Scenario S3 When the mutation throws a tantrum

To those who tried to create a model in a spreadsheet last year and failed miserably, I just say no, you can't get a complete dynamic solution. And finally for those who didn't know at first; if you still have no idea what it should be done with the grandma in Pardubice, please look for an office that fits your talent better. Something like mp, or any place where stupidity is a plus.

The ancient pilgrim once looked upon the mountains, from where he hoped the help will come. We modern people, with an university-issued *piece of paper*, often of a master's level, tend to condemn such behavior: "What a foolish idea, to expect help from a pile of stones and clay!" But the general public hopes in entities that lack **everything what is needed** to fulfill the hope, and the only thing those entities have in excess is unsubstantiated self-confidence. Forgive me, but in this context the pilgrim's actions seem highly rational. So don't blame me for following his example.

Reference
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