**Title:f**

**A mathematical model of virus population growth dynamics on the basis of activity spread in permeable networks.**

**Author information:**

Peter Krall1, Christoph Krall2

1 Corresponding author. Dr. Peter Krall Consulting, pk@peter-krall-consulting.de  
2Vienna Medical University: christoph.krall@meduniwien.ac.at

# Abstract

Activity spread in networks is modeled. The networks are embedded in a pool, and they are permeable in the sense of disconnecting nodes and replacing them with nodes from the pool at a rate corresponding to 5%-50% exchange during node activity periods. Depending on the model parameters, this results in initial waves, followed without change of environmental constraints by transition into a steady state with nonzero activity. Additionally, active strains are rather rapidly eliminated and replaced by more aggressive intruders. These characteristics of dynamics are mirrored and multiplied in pools where permeable networks are embedded if spread in these pools is largely confined to spread in stable networks with low random network-to-network activation probabilities. It follows for epidemiology that chains of nosocomial transmissions, or perhaps transmission chains in other semiclosed groups, can start with initial waves and then fall back to a prolonged near-steady state, can support the persistence of a virus, and can enable rapid replacement of a wild type by a more aggressive emergent strain. Activity in the community mirroring these patterns can be stimulated if transmissions are rare in settings where random contacts occur but frequent in settings where some stable groups gather.

**Keywords**

Network epidemiology, temporal networks, mathematical analyses, computational modeling, COVID-19.

**A mathematical model of virus population growth dynamics based on activity spread in permeable networks.**

# Abstract

Activity spread in networks is modeled. The networks are embedded in a pool, and they are permeable in the sense of disconnecting nodes and replacing them with nodes from the pool at a rate corresponding to 5%-50% exchange during node activity periods. Depending on the model parameters, this results in initial waves, followed without change of environmental constraints by transition into a steady state with nonzero activity. Additionally, active strains are rather rapidly eliminated and replaced by more aggressive intruders. These characteristics of dynamics are mirrored and multiplied in pools where permeable networks are embedded if spread in these pools is largely confined to spread in stable networks with low random network-to-network activation probabilities. It follows for epidemiology that chains of nosocomial transmissions, or perhaps transmission chains in other semiclosed groups, can start with initial waves and then fall back to a prolonged near-steady state, can support the persistence of a virus, and can enable rapid replacement of a wild type by a more aggressive emergent strain. Activity in the community mirroring these patterns can be stimulated if transmissions are rare in settings where random contacts occur but frequent in settings where some stable groups gather.

**Keywords**

Network epidemiology, temporal networks, mathematical analyses, computational modeling, COVID-19.

# Introduction

Network models can represent the dynamics of virus spread on a level of abstraction that allows to study the characteristics of the dynamics depending on the characteristics of the connection graph and, in some models, the change in the connection graph over time [1, 10, 11, 12, 16, 18].

One class of network models is based on stable networks and studies how the characteristics of spread dynamics depend on the density of the networks [10, 18]. These models show that growth closely resembles compartmental models with random mixing if the density is high. Conversely, initial fast growth is followed by prolonged periods of nearly constant new cases if the connectivity is low. Positional effects can also result in growth dynamics that more closely resemble the expansion of a wildfire than logistic growth [11, 19].

Apart from the appearance of steady states, the growth and collapse of virus populations from the COVID-19 family revealed that the intrusion of a more transmissible strain can lead to the elimination of the previous wild-type strain rather rapidly; for example, none of the thousands of active B.1.7 cases in Denmark, week 21, 2021, had a continuation long enough to trigger a new case in week 31, whereas B.1.617.2 numbers increased from 31 in week 21 to 5427 in week 28, subsequently plateauing [5, 13] [Table 1].

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Week | Cases | seq. | B.1.1.7 | B.1.617.2 |  | Week | Cases | seq. | BA.2 | BA.4 | BA.5 |
| 22-21 | 5701 | 4445 | 4394 | 31 |  | 20-22 | 3845 | 2905 | 2766 | 52 | 85 |
| 23-21 | 2845 | 2485 | 2418 | 64 |  | 21-22 | 3079 | 2236 | 1836 | 83 | 317 |
| 24-21 | 1669 | 1361 | 1267 | 87 |  | 22-22 | 3487 | 2246 | 1440 | 113 | 693 |
| 25-21 | 1327 | 1166 | 813 | 340 |  | 23-22 | 5136 | 3770 | 1719 | 281 | 1770 |
| 26-21 | 2704 | 2310 | 821 | 1473 |  | 24-22 | 7150 | 5865 | 1721 | 464 | 3678 |
| 27-21 | 4680 | 3223 | 578 | 2635 |  | 25-22 | 8780 | 4481 | 834 | 349 | 3298 |
| 28-21 | 6900 | 6177 | 423 | 5742 |  | 26-22 | 10801 | 4246 | 450 | 304 | 3491 |
| 29-21 | 5338 | 4636 | 156 | 4473 |  | 27-22 | 12339 | 3928 | 272 | 308 | 3342 |
| 30-21 | 6344 | 5582 | 62 | 5518 |  | 28-22 | 12061 | 3556 | 110 | 222 | 3219 |
| 31-21 | 6445 | 5492 | 39 | 5452 |  | 29-22 | 10262 | 4008 | 75 | 238 | 3698 |

Table 1 Episodes of wild-type replacement in Denmark, week 22--21 > 31--21 and 20--22 > 29--22

The rapid collapse of a previously stable virus population after the arrival of a new strain is not self-evident because the growth dynamics of virus populations in a host population, whether they descend from a recent common ancestor or not, are only directly coupled by their impact on susceptibility—a Covid B.1.1.7 case will, with the rare exception of mutation or simultaneous infections, not have B.1.617.2 successors. Indirectly, appearance of a new strain may also influence environmental constraints for the previous wild-type if it causes behavioral changes but this is not plausible for several processes of Covid-19 virus population replacements by other populations from the Covid-family, for example not for B.1.1.7 replacement by B.1.617.2 in Denmark at a time when there were almost no restrictions, and particularly no tightening of restrictions [8]. Therefore, why should B.1.1.7 collapse at a level of susceptibility caused by the spread of both strains if it would not collapse at this level resulting from the spread of B.1.1.7 alone?

Wild type replacements similar to those in Denmark have been observed throughout Europe [5]. Whether this is specific for Covid-19 family populations or has just been missed elsewhere because of a lack of systematic sequencing for other virus families is unknown, but in any case, viable epidemiological models must be consistent with rapid collapse of strain populations soon after intrusion of a more aggressive strain, as well as being consistent with steady states after initial waves. Computer experiments have shown that rapid wild-type replacement is possible if a virus is endemic in a semiclosed population such that membership is neither ultra-short nor permanent, and leaving members are replaced by new arrivals from an external pool, such as the populations of residents in hospitals [12]. These experiments also show waves and steady states. This motivates this paper’s approach of formalizing and studying a model of networks called ‘permeable’ because the exchange rate corresponds to something between 5% and 50% during a node’s active period. We will also discuss how, and under what conditions, compounds of permeable networks can exist and how, and under what conditions, they can drive and modulate the dynamics in a much larger pool.

# Model

The model presented is hoped to help understand what is happening in reality, but it is much simpler than reality, and the link between model language terms and measurable observables is not sufficiently rigid for a formal representation of natural systems in the sense of physics or chemistry [17]. Therefore, the model will be explicitly introduced as a formal construct, postponing the epidemiological interpretation to the discussion.

## 2.1 Permeable Network Models:⬄ PNM

A PN model essentially is a formal construct specializing the well-known SEIR model. What is specific is the focus on studying effects of permeability in the sense that considerable fractions of nodes are replaced by nodes from an external pool at a rate somewhere in the range of 5%-50% in the period of any node’s activity. It is intuitively plausible and will be proven in the results section that such exchange rates in combination with sufficient transmission probabilities can result in a steady state where a constant fraction of newly added nodes will be activated by currently active nodes in the system.

In addition to the conditions leading to the existence of a steady state of nonzero activity and the characteristics of the trajectories from low activity to such states, the replacement of an activity strain by an intruding strain is another topic to be modelled. Therefore, PMNs can optionally include two strains, ‘Strain X’/’Strain Y’..

The model is deterministic, and the states of the network are defined as fractions of nodes in various possible states. The network state changes in an iterated three-step cycle, optionally disturbed by special transitions.

In the initial exposition step, some nodes change from the initial state to the triggered state. The fraction of nodes triggered depends on the fraction in the initial and active states, the number of pairwise connections opened in the step, and the fraction of opened connections resulting in transmission. The number of opened connections is given by a model parameter *nc*, interpreted as follows: There are *nc* iterations of connecting nodes; in each iteration, each node is connected to exactly one other node. The fraction of connections causing triggering among open connections between a node in the initial state and an active node is given by a model parameter for the single-strain variant and , for two strains. A variant of the model also allows different values for depending on the number of steps active nodes advanced within their active period, representing nonconstant levels of activity.

Only nodes in the initial state can be triggered, and by being triggered, their state changes immediately, implying that subsequent contacts with active nodes have no effect. The probability of a node in initial state not to be triggered is thus the product of probabilities not to be triggered by either strain. Triggered nodes do not get active immediately and active nodes remain active for all iterations of the exposition step, implying that the active fraction remains the same for all iterations of the exposition step-

Writing , for the currently active fraction of nodes, for nodes in the initial state, and for the new triggered fraction, transmission for the single strain is defined as follows:

Note, that , ensuring that for a sufficient number of contacts almost all nodes introduced in the initial state will which enter the network will be triggered immediately after introduction.

If there are two competing strains, the transitions are given by:

1. *pnewX* + *pnewY :*=
2. *pnewX*=(*pnewX*+ *pnew*)
3. *pnewY*=(*pnewX*+ *pnew*)
4. In the second step, nodes in the triggered state advance one step toward activation, and nodes in the active state advance one step toward the final state. For the single-strain variant, the number of steps in the triggered state before becoming active is defined by a model parameter τtr, and the length of the active period is defined by the parameter τact. The corresponding parameters for the two-strain variant are τtrX, τtrY, τactX, τactY.
5. In the third step, a fraction of nodes on the network are replaced by nodes in the initial state drawn from an external pool, and another fraction is replaced by nodes in the final state drawn from the external pool. The size of the fractions is given by the model parameters , . The replacement probability is the same for nodes in any of the different possible states. In particular, the proportions of nodes in different stages of advancement among triggered and active nodes remain the same.

The basic model considers the fractions of nodes arriving from the pool in either initial or final state constant, ignoring the impact of exchange between the permeable networks and the pool on the fractions of nodes in the initial and final states within the pool. The rationale is that we want to show that patterns, particularly falling back from initial peaks to lower steady activity levels and rapid replacement of activity strains, do not depend on the change in the pool and will, in other words, also occur if the pool is so much larger than the networks that effects of exchange in the pool are [negligible](https://www.linguee.de/englisch-deutsch/uebersetzung/negligible.html) for short and medium periods.

1. In the two-strain variant, the second strain will initially not be present. At some point, some of the nodes in the initial state can be switched to triggered by this strain. Other optional steps concern changes of model parameters for the subsequent iterations.

The simple model could obviously be generalized in many ways, particularly by considering changes in the pool, considering several strains, or replacing the ‘final’ state with a state that is only temporarily not triggerable but that would require heavier formalization, which is not necessary for the questions addressed here.

## 2.2 Embedded Permeable Network Models:⬄ EPNM

In the basic PNM, the environment is considered only a source of nodes in the initial or final state and absorbs the replaced network nodes. However, we are also interested in how PNM activity can stimulate and modulate the activity in the pool if this pool is also a system of networks, and in addition to the PNM, a node triggered in the PNM will also become a possible source of activity outside the PNM.

The EPNMs of this paper are rather simple aggregations of networks linked to PNMs or compounds of PNMs via a stimulation function. The focus will be on the following questions: under what circumstances will stimulation result in multiplication rather than self-sustained logistic growth, and when will replacement of active strains in the PNMs cause replacement in the stimulated pool soon after replacement in the stimulating permeable networks?

# Results

This section studies some characteristics of PNMs/EPNMs by applying both mathematical analyses and computational methods.

## 3.1 Single-strain systems

The first group of results concerns the trajectories of activities in PMNs from low levels to a steady state where only a single strain of activity is present. Examples of parameter combinations were simulated via C++ programs. The equations defining fixpoints were derived from the model definition and solved for parameter combination examples via Mathematica.

### 3.1.1 Persistence of activity

If there is a single strain and if there is a nonzero exchange rate including a nonzero fraction of nodes in the initial state, if the transition probability per contact event is nonzero, and if there is at least one active state and if the length of the triggered, nonactive period is finite, then there is a number of iterations of the transmission step such that the zero-activity fixpoint is repelling.

Proof: The simplest proof is by contradiction:

After the replacement step at any iteration *t*, there will be at least nodes in the initial state. If any part of them is triggered, then at time *t*+1+τ.tr, there will be nodes that were added to the network at iteration *t* and triggered immediately, which just became active at time *t*+1+τ.tr. Therefore, is a lower bound for active nodes at iteration *t*+1+τ.tr. By choosing a sufficiently high value for *nc*, it can be assured that this lower bound is sufficient for more than to be triggered at iteration *t*+1+τ.tr, which implies that again will be a lower bound for active nodes after another τ.tr iterations, and so on for *t*+1+2τ.tr, *t*+1+3τ.tr,… If the activity period has at least length 2, then it is also straightforward that gaps between iterations with nonzero activity cannot be permanent.

Corollary: If there is a nonzero fraction of active nodes at any iteration *t* and if the length of the activity period is at least 2, then for every nonzero and any number n>1, there are values for *nc* and a number k such that will become a lower bound for triggered nodes in any iteration after *t*+k. This follows immediately from the proof above.

Remark: This does not prove the existence of a nonzero attractive fixpoint for all parameter values, implying that the zero-activity fixpoint is repellent. Actually, there are (somewhat exotic) systems with periodic fluctuations.

### 3.2 Fixpoints of activity

Since the fractions of nodes remaining in the network decrease as a geometric series and as the number of new triggering contacts is constant at the fixpoint, this (before the transmission step) can be characterized by the following equations for , denoting fractions of nodes in initial, respectively active state at start of the exposition step, and denoting new triggering events at the fixpoint.

The change of nodes in initial state at time is given by the proportion of nodes in the initial state introduced into the network ,the proportion of nodes in initial state which are triggered in generation and remain in the network after exchange, and the proportion of nodes in the initial state which survive the exchange step and can be described by the following difference equation:

which in equilibrium obtains

Nodes in the active state are those that were added in the initial state, became triggered, past the period before activation, and did not yet change to the final state:

Also,

which obtains in equilibrium

With

this combines to:

The equation has a trivial fixpoint at = 0. There is a nonzero solution in the interval (0,1] if the sum of a triggered node’s chances of reaching any of the active states, multiplied by the number of nodes triggered in one iteration by an active node, will be above 1. For given parameters and minimal values for and can be derived to allow a stable equilibrium. For example, at the beginning of the epidemic when there are no nodes in the final state in the external pool, implies triggering of ≈ 0.013 nodes per iteration; later on, when a fraction of the nodes newly introduced into the PN in each generation is already in final state, the rate of new infections will be smaller: for and otherwise, identical parameters reduce to approximately .

If the active period is at least of length 2, then for every >0, >0, and δ>0, the lower bound for the triggered fraction in each generation will eventually become greater than --δ for sufficiently high values of *nc*. The proof is analogous to the proof of the repellent nature of the zero-activity fixpoint for sufficiently high values of *nc*. The only additional constraint required is the length of the activity period because for , gaps in the series of activations will never be closed.

### 3.1.2 Waves of activity

PMN activity does not approach the quasisteady state on a smooth path but rather in a sequence of waves. The effect can be very strong or moderate, depending on the model parameters, as will be demonstrated by the examples below. The effect as such, however, is inevitable if the network starts at a low level of activity. The reason is that the number of nodes in the initial state will be greater than that in the network’s steady state when the number of active nodes first approaches the steady-state value because fewer nodes will have been triggered in the preceding iterations, implying a subsequent maximum higher than the steady state. Eventually, the fraction of triggered nodes will exceed the value at the network’s quasisteady state because the temporary presence of more active nodes causes more triggering. Therefore, , resulting in , a consequent reduction of the proportion of newly activated nodes to the value at the network’s steady state, or even below. Thus, there will be a local minimum below the steady-state value. Calculations with various parameter settings display such waves as shown inFigures 1--3.

|  |  |  |
| --- | --- | --- |
| Fig 1 New triggerings per cycke in  computer simulations with parameters of scenarios 1-6 | Fig 2  Newly triggered fraction, fraction in initial state, and active fraction of scenario 1 | Fig 3  Strong fluctuations of new cases per cycle in a scenario with short active period and high exchange rate (scenario 7) |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | Scenario |  | ptrans | *Nc* |  |  |  | | 1 | 0.025 | 0.03 | 20 | 4 | 3 | 0 | | 2 | 0.06 | 0.03 | 20 | 4 | 3 | 0 | | 3 | 0.06 | 0.12 | 20 | 4 | 3 | 0 | | 4 | 0.12 | 0.03 | 20 | 4 | 3 | 0 | | 5 | 0.12 | 0.12 | 20 | 4 | 3 | 0 | | 6 | 0.015 | 0.03 | 20 | 4 | 3 | 0.01 | | 7 | 0.2 | 0.125 | 40 | 2 | 4 | 0 | | | |

The most obvious differences between the PN-Model and random-mixing compartment models concern the appearance of a steady state and the preceding local maxima and minima, with values significantly different from those at the steady state. For low exchange rates, factors of 4.0+ between the first maximum and the following local minimum are observable, with the steady state being closer to the local minimum. High exchange rates and short periods of activity generate zig-zag trajectories [Figure 3].

Neither the first maximum nor the growth rate allows the prediction of the level of activity. In particular, a lower exchange rate may result in faster initial growth and higher maximum but lower activity at steady state than a model with a higher exchange rate and otherwise identical parameter values (runs 1 and 2 in the examples).

There is no theoretical limit for the factor by which the first maximum of the new triggered fraction exceeds the value at the quasisteady state, as seen from the following thought-experiment: If the system starts with all but a small fraction δof nodes in initial state, then high values for , *nc* will result in immediate triggering of a fraction close to 1-δ, regardless of the value of , But the fraction triggered per iteration in steady state is limited by , which can be arbitrarily small

### 3.1.3 Periodic attractors

If there is only one active state or if all but one state has a very low transmission probability, then the attractor for the system dynamics can be periodic with a repelling inner fixpoint.

A simple example is , , , , The system starts with 0.00009 (or any other low, non-zero value) in active state and 0.00009 8or any other low, non-zero value) nodes in triggered state in generation 0, the other nodes in the network being in initial state. Since , , the nodes being active in generation 0 will have active successors in generations with index 2n, the nodes being in triggered state will have active successors in generations 2n+1. As almost the whole network initially in initial state, active nodes in either state will initially have active successors 2 generations later, so the sequences of new triggering in generations 2n as well as those of new triggering in generation 2n+1 will initially grow. However, when the values for and both approach 0.0115/2, the even sequence wins, because higher proportions of nodes activated in even sequences leave less nodes in initial states for triggering in uneven generations. The attractor for this system is periodic with a length of 2 and values of every other iteration and between. The role of even and uneven generations can of course be swapped, depending on the initial frequencies of active and triggered nodes.

Calculating the next elements after an assumed alteration of for even and for odd indices shows why the periodic trajectory is locally attractive, and that the transition to a pulsing state of the network observed in numerical simulations is not an artifact: In even generations, the proportion of not in initial state can be obtained as convexcombination of geometric sums of nodes in initial state introduced in even generations not triggered and not exchanged and analogously for uneven generations with as proportion of nodes not exchanged in a 2 generation cycle; of these two sequences, the first will begin with a proportion of nodes in active or final state and triggered in even generations, and nodes in active or final state triggered in uneven generation. The second component is derived analogously, with the exponents of the proportions of triggering changing their positions.

In this case, the next even index element triggers a fraction

The fraction triggered at the next odd index will be

The values for even indices thus increase further until they reach , whereas odd index values approach 0. Since there are non-zero intervals between and , respectively between and , modifying the model by adding a small but non-zero fraction of active nodes among those joining the network from the pool will merely shift the values of and but the pulsing characteristic will prevail. This also holds for modifying the model by assuming a small for transmission probability generation +1 after triggering

Another example of a pulsing network is , , , , and for the first active state and 0.5/73 for the second active state. This system produces waves of length 3. Since the value set of C++ long double is finite, the numerical simulation must eventually become periodic, but more than 108 iterations are needed. For example, values for new triggering after to are the sequence

0.00339078, 0.0153953, 0.00156011 | 0.00340107, 0.0153922, 0.00155286 | 0.00341139, 0.015389, 0.00154567

While the practical relevance of pulsing networks is disputable, their existence shows that there need not be a globally attractive inner fixpoint in cases where the zero-activity fixpoint is repellent

### 3.1.4 Effects of reducing the number of contact events

Different numbers of contact events for otherwise identical model parameters usually correspond to different nonzero steady states of activity. Consequently, a change in the contact event number parameter in the dynamics of a PNM will cause a response but often does not cause the system to approach zero activity. An example is shown in [Figure 4]: the reduction of *nc* from 20--4 after the system becomes stable at triggers an immediate decrease to , followed by a rebound to , followed by another decrease to before eventually stabilizing at after some further increase and decrease. An observer trying to understand the network on the basis of the assumption of random contacts in a closed system would probably assume that activity should soon come to a halt after falling to from and feel tempted to propose all kinds of ad hoc explanations for what follows; however, for a PMN, this is a normal response to changes in environmental constraints.

The decline will be gradual if the contact reduction is gradual, but the transition to a new steady state will also occur after a possibly rather fast decline that could, on the basis of random-mixing SEIR models, be mistaken for indicating imminent elimination of activity under the environmental conditions where the decline happens.

### 3.1.5 Reduction of nodes in the initial state in the pool

The PN model also allows us to account for changes in the pool with respect to the proportion of nodes in the final and initial states. This also causes the transition to a lower level, but again, the initial fall does not necessarily precede a subsequent approach to a zero-fixpoint. The decline will be gradual if the reduction in nodes in the initial state is gradual [Figure 5], but the transition to a new steady state will also occur after a possibly rather fast decline that could, on the basis of random-mixing SEIR models, be mistaken for indicating imminent elimination of activity under the environmental conditions where the decline happens.

|  |  |
| --- | --- |
| Fig 4  Responses to sudden or gradual reduction of contact contact events per cycle | Fig 5  Responses to reduction of fraction of nodes in initial state in the pool nodes are exchanged with |
| |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | | Scenario |  | ptrans | *nc* |  |  |  | *reduction steps* | | 8a | 0.06 | 0.12 | 20→4 | 4 | 3 | 0 | 1 | | 8b | 0.06 | 0.12 | 20→4 | 4 | 3 | 0 | 25 | | 8c | 0.06 | 0.12 | 20→4 | 4 | 3 | 0 | 50 | | 9 | 0.06 | 0.12 | 20→2 | 4 | 3 | 0 | 50 | | 10a | 0.06→0.018 | 0.12 | 20 | 4 | 3 | 0→0.042 | 1 | | 10b | 0.06→0.018 | 0.12 | 20 | 4 | 3 | 0→0.042 | 25 | | 10c | 0.06→0.018 | 0.12 | 20 | 4 | 3 | 0→0.042 | 50 | | |

## 3.2 Strain replacement

The second group of results concerns trajectories for the activity of two strains, one being present from the beginning and the second intruding later when the first strain has reached a steady state. The restriction to scenarios where the first strain had enough time to reach steady state is purely pragmatic; modeling the abortion of the first strain’s ongoing initial growth is possible in the PMN framework but is not studied here.

### 3.2.1 Strain replacement by a more transmissible strain

The equation characterizing the fractions of triggered nodes implies immediately that a strain with a higher transmission probability will be able to invade a PN and cause the collapse of the previously stable strain. This confirms the results of computer experiments based on similar concepts, although a somewhat different formalism is used [12].

Replacement as such follows immediately from the definition: if Yis more transmissible than X, then at any point, the proportion of nodes triggered by active nodes of strain Yamong all triggered nodes will be greater than the proportion of active nodes of Yamong all active nodes. If the lengths of the preactive and active periods coincide for Xand Y, the overrepresentation of Y among triggered nodes will subsequently propagate to active nodes.

There is a characteristic pattern in the trajectory of the previously persistent strain: Initially, the factor from generation to generation will be close to 1, and then, the factor will accelerate until it reaches a near-constant factor. In scenario 13 [Figure 6], is reduced from 0.0180019 to for the first 40 iterations after the system is seeded, and from to 0.00383989 for the next 40 iterations. The simple explanation is that the strains affect each other’s activity only by reducing the fraction of target nodes in the initial state. The negative growth rate of strain Xtherefore reflects the level of activity of strain Y, not the growth rate of Y.

The growth curve of the intruding strain can be smooth or show an initial peak (scenario 11 vs 14, Figure 6). Reduction of contact events before intrusion of strain Y will reduce activity at steady state but may increase the height of the initial peak as the reduced activity of strain X yields a higher fraction of nodes in initial state at the system’s steady state before intrusion of X (scenario 11 vs 12, Figure 6).

### 3.2.2 Strain replacement by a strain becoming active earlier

There is strong selective pressure on the delay between being triggered and becoming active in PNs. This results from the impact of replacement, which reduces the fractions of triggered nodes in each iteration. The parameter examples [Figure 7] show that a shorter delay before becoming active can—in a setting with a high exchange rate—overcompensate significantly lower transmissibility.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Fig 6  Scenarios of replacement of an activity strain by another one with higher transmission probability per contact event. | | | | | | Fig 7  Replacement of an activity strain by another one with shorter time to become active, scenario 15. | | | | | | |
| scenario | *nc* initial | *nc* reduced |  |  |  | |  |  |  |  |  | intrusion strain Y |
| 11 | 5 | - | 0.04 | 0.0 | 0.14 | | 2 | 3 | 0.25 | 2 | 3 | 400 |
| 12 | 5 | 3 after 200 | 0.04 | 0.0 | 0.14 | | 2 | 3 | 0.25 | 2 | 3 | 500 |
| 13 | 5 | 3 after 200 | 0.04 | 0.0 | 0.14 | | 2 | 3 | - | - | - | - |
| 14 | 5 |  | 0.04 | 0.0 | 0.14 | | 2 | 3 | 0.18 | 2 | 3 | 300 |
| 15 | 40 | - | 0.2 | 0.0 | 0.125 | | 4 | 2 | 0.1 | 2 | 2 | 150 |

### 3.2.3 Strain replacement or coexistence with asymmetric inhibition

If nodes activated by strain X after the active period reach a state that still allows being triggered by strain Y but is not triggered again by X, while nodes triggered by Y enter a final state that cannot be triggered either strain, and if other parameters are such that X would be eliminated after the appearance of Y with symmetrical inhibition, then elimination with asymmetric inhibition will be faster. This follows immediately from the consequence of asymmetric inhibition that Y can spread faster if nodes previously triggered by X can be triggered by Y after their active period has ended, which speeds up the process of reducing the fraction of nodes that can be triggered by X.

Asymmetric inhibition can but need not lead to stable coexistence if other parameters are such that X would not be eliminated after the appearance of Y with symmetrical inhibition. Coexistence will result if the sum of the fraction of nodes in the initial state plus the fraction of nodes after strain-X active period is high enough to allow Y to invade. This can occur if  , because the fraction of nodes that can be triggered by Y is greater than the fraction of nodes that can be triggered by Y. However, Y will then reach a steady state where the fraction of nodes in the initial state is higher than the minimal fraction for X to survive. On the other hand, the advantage of resulting from asymmetric inhibition is limited if nodes in the active or preactive X-state cannot be triggered, implying that asymmetric inhibition can but does not always compensate for other disadvantages.

Partial inhibition in one or both directions or time dependency are further possible complications.

## 3.3 Embedded permeable networks

This section concerns systems where permeable networks are embedded into accounts of such networks. The considerations are argued but without formalization where the conclusion is qualitatively obvious and details are not very relevant.

### 3.3.1 Compounds of permeable networks

A compound of permeable networks is understood as a mesh of networks connected in the sense that, for some indexing by pairs of natural numbers, reaching some level of activity in any network will cause a spillover to adjacent networks, but activity flow between networks always remains low. The idea is that staff members, travelers, patients transferred to one hospital to another, or patients admitted to a hospital after infection in another hospital where they have been for whatever reason, preachers, etc., can seed a network but will not make a major contribution once the activity in the second network has started.

The speed of activity propagation in a compound depends on the length of the period before a triggered node becomes active and on the level of activity that must be reached before spillover. Argument: If a network with index has been triggered at some time *t* from an adjacent network and seeds an adjacent network with index at time *t*’, then they will essentially proceed on their trajectories in parallel. An analogous argument holds for propagation of strain replacement.

The consideration is rather trivial but noted because of the implied possibility of rapid propagation of an activity strain through a compound of permeable networks, which may explain the patterns of intruding strains’ propagation observed in spread of virus populations from the Covid-19 family [Figure 9].

### 3.3.2 Compounds of permeable networks embedded in randomly connected pools

Embedding compounds of permeable networks in a randomly connected pool means the introduction of an average number *r* of follow-up triggering events in the pool where nodes are drawn from and returned to. This process is stimulated by returning active nodes from the networks to the pool and optionally by an additional stimulation function. Strictly speaking, this will change the proportion of nodes in the final versus initial state in the pool, but if the pool is much larger than the networks and if , this change will be slow.

If is outside the PNs, then there will be self-sustained logistic growth in the pool. In this case, in-pool activity transmission will soon dominate if the pool is much bigger than the permeable networks. For spread as such, that implies that steady states and prolonged phases of fluctuations of new activation numbers with several local maxima and minima are virtually impossible, just as they are without permeable networks to start with. Additionally, there is no reason for the elimination of a dominant strain before the fraction of nodes in the initial state becomes low. The appearance of a more aggressive strain will speed up the reduction of nodes in the final state, but that is all does. Only if the more aggressive strain appears by some strange coincidence shortly before the predecessor was going to disappear anyhow will elimination of the predecessor occur shortly after the appearance of the successor but before a significant reduction in nodes in the initial state.

If is outside the PNs, then propagation through the pool will result in multiplication of the activity in the compound of permeable networks. In theory, the factor can be arbitrarily high if for some sufficiently small or if active nodes in the network have many direct successors outside. However, a value of close to 1 implies that the system is always close to starting logistic growth. Additionally, such values are incompatible with rapid replacement of a previously dominant strain because they allow for long transmission chains, for example, ; thus, if the proportion of nodes in the initial state does not change drastically in the respective period, the value of corresponding to a 10-fold multiplication of cases in the nets implies that 15% of the initially dominant strain 20 generations after it has been eliminated from the permeable networks. More generally, if the average number of successor nodes in a set of graphs outside the permeable network does not depend on the distance from the last node in the permeable network and if nodes can appear only once in the graph, then the average number is given by the sum of the geometric series, and the fraction of chains of some length *l* or above is given by the *l-th* power of the coefficient. Applying this basic mathematical rule to spread graphs rooted in triggering nodes from permeable (or other) networks yields that strain replacement cannot be fast in a scenario where the total activity is a multiple of activity in the permeable networks by a high value of the multiplication factor unless there is a strong negative correlation between average successors and distance from the root.

### 3.3.3 Spread in a pool with embedded permeable and stable networks

|  |
| --- |
| Fig  A stable network that will result in a high secondary attach rate while possible transmission chains will be short. |

When the root of the spread graph outside the permeable network, i.e., the root of the complete spread graph’s continuation outside the permeable network compound, is an element of a stable network, there will be a negative correlation between the number of successor nodes and the distance from the root. This can result in a high number of activations without triggering self-sustained growth in the pool. Figure 8 shows an example of a stable network template: if any node in this structure is temporarily integrated into a PN’s connection web and activated there, there will – with sufficient transmission probabilities – be many successors since the multiple connections between nodes outside the central hypercube to nodes in this hypercube will imply the hypercube’s activation, which will in turn result in activation of most of the remaining nodes. Nevertheless, the longest possible chain in the compound is 7 in length, implying that activity will be a violent but short-lived outburst. Also, adding more nodes connected to the central hypercube but not to each other will increase the expected number of activations ut not the maximum path length,

The example shows an engineer’s solution. Simple and immediately understandable solutions do not have a particularly plausible direct interpretation. Nevertheless, these experiments show that PN-driven spread can modulate spread in a much larger pool and that the modulated spread can simultaneously be a multiple of the modulating spread, allow for steady states, allow for waves after changes in environmental conditions, and allow for rapid elimination of an active strain after a more aggressive strain intrudes.

Apart from the existence of stable networks, another constraint for the possibility of a scenario where an activity strain can be replaced rapidly while activity is a multiple of activity in the stimulating PN compound is the absence of a strong random component that would cause network-to-network activation, resulting in logistic growth of the number of activated networks. Since many nodes are activated once a stable network is triggered and since other networks consist of many potential target nodes and since the density of networks must be sufficiently high to yield a relevant fraction of the nodes in the PNs at any time to be elements of a stable network, this is a strong constraint.

# Discussion

On the basis of the analogy between network nodes and cases in virus spread dynamics, we propose and subsequently discuss the conjecture that EPNMs are plausible models for the spread of some virus types. This EPNM-conjecture refers to data on the spread and collapse of strain populations from the Covid-19 family as the Covid years, for all their annoying aspects, generated many data.

## 4.1 Preconditions for a plausible epidemiological interpretation

The first step for establishing the epidemiological interpretation will be to show that the model assumptions can reasonably be mapped to reality. This concerns the correspondence between nodes and cases, between networks and populations, and between network isolation and population segmentation.

### Interpretation of nodes as cases

Interpreting nodes as abstract representations of cases of virus infection establishes the correspondence between the network model and well-known SEIR models. The specific novelty of the EPNM approach concerns the groups of individuals where transmissions occur, not the virus characteristics as such.

### 4.1.2 Existence of scenarios corresponding to permeable networks

There is at least one well-studied class of populations left and joined by individuals at a rate consistent with the PNM assumption: residents of hospitals. Additionally, nosocomial transmission is known not to be uncommon, and seeding of activity in one hospital can occur through a variety of mechanisms, including the transfer of patients, the admission of a patient who became infected in a hospital where they were for whatever cause to another hospital, or staff working in two units of the healthcare system [4, 16]. These mechanisms may not cause much flow, but since seeding is all that is required to trigger spread in a permeable network, they can be sufficient.

There may be other candidates, such as religious services or weekend clubbing events, but for the purpose of this paper, one plausible real-word interpretation of PN compounds is sufficient.

### 4.1.3 Possibility of segmentation

The superposition of spread in stable networks and transmissions in random contact events will almost inevitably result in fast logistic growth unless either stable networks are rare or transmissions in random contact events are rare. This raises the question of whether the high degree of separation required by EPMNs to explain the rapid elimination of previous wild types is plausible and how it can be explained.

Regarding the plausibility of segmentation, the data show the dynamics of C-19 B.1.617.2 allowed for sequences of weekly cases such as 6823, 5299, 6256, 6360, 5675, 5292, 2937 (Denmark, Weeks 28--34 2021; B.1.617.2 was almost 100% dominant, mask mandates were phased out from June 14th and lifted completely September 1st), or the original strain allowed 3229, 3740, 3752, 4203, 3832, 4153, 3869, 3659, 4280 (Sweden Weeks 14--22 2020, masks neither mandatory nor common) [5]. Independent of the EPNM conjecture, the connectivity of populations in terms of transmission probabilities allows for prolonged phases of near constant activity [10, 18]. This is not proof of the EPNM conjecture but weakens a possible objection, as it shows that activity need not yield logistic growth and that the separation required by the EPNM conjecture is possible.

On the other hand, there have been massive outbursts in choir rehearsals or religious gatherings or in groups working in particular settings such as slaughterhouse crews [3, 7, 8, 13]. An obvious conjecture is a very strong dependency of infectiousness on an individual’s state, not only in terms of being symptomatic or not but also in terms of being excited by setting-dependent activities such as singing, praying, dancing, continued speaking, or physical work. If this is the case, then stable networks can be separated if their members do not engage in activities where their bodies are in the excited state but meet only in settings where there is no relevant transmission probability.

## 4.2 Patterns in the dynamics of virus populations from the COVID-19 family

The final step for establishing the plausibility of the epidemiological interpretation will be to show that the model’s characteristics match the empirical data.

### 4.2.1 Strain replacement

The sequencing of genomes allowed to distinguish the dynamics of different virus populations from those of the C-19 family. This led to the following observations, which motivated the conjecture underlying this study: virus populations collapsed after the intrusion of an emergent strain, and they often did so before the population immunity resulting from the simultaneous growth of both populations reached a level where the previous wild type would be expected to disappear without the successor’s intrusion. The growth of the more aggressive strain population is not surprising, but the collapse of the previous wild type after a moderate increase in immunity requires an explanation.

While rapid elimination of previous wild-type strains has been observed repeatedly throughout Europe, the elimination of B.1.1.7 and BA.2 in Denmark is particularly well documented [5] [Table 1]. Between mid-May 2021 and the beginning of August 2021, B.1.1.7 all but disappeared, whereas B.1.617.2 thrived between mid-May 2021 and the end of June 2021 to become almost stable afterwards until the end of August 2021, BA.2 was eliminated by BA.5 one year later. NPIs are not an explanation for the decline, as there was no tightening of rules in the relevant period. Vaccinations played a role, but the increase from ~24% in mid-June to ~40% in mid-July could hardly explain the rapid decline in new cases. In the PMN model, the decline in weeks 22--21 to 24--21 could be part of the wave that started 53--20, while the rebound was blocked by B.1.617.2, even though the immunity in the population as a whole cannot have changed much.

There were also strong positional effects in the replacement processes [20][Figure 9]. This resembles the expected dynamics of EPNs if the pools of the PNs in the compound are defined by the vicinity to the place of residence associated with the respective PN.

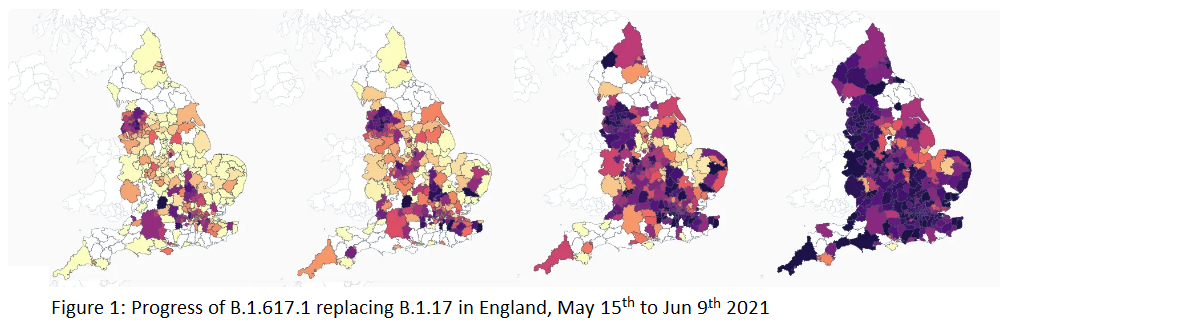


Figure 9

Progress of B.1.617.1 replacing B.1.1.7 in England, May 15th to Jun 9th 2021

### 4.2.2 Transitions from peaks to fluctuations in bands and sometimes prolonged periods of quasisteady state

There were periods when case numbers first increased significantly, then reversed and changed to fluctuations. After the decline, the activity stabilized rather than falling to very low residual levels, as random-mixing models would predict but also did not return to the previous maximum until a new strain emerged [14][Figures 10-13]. Italy, weeks 21--50. 2022 is a particularly informative example because the rules were relaxed rather than tightened, so the inflection point in the middle of July cannot be attributed to interventions. Rather, the increase from 139k/week 22--21 to 665k 22--28 coincided with the replacement of BA.2 and BA.4 by BA.5, followed by the characteristic post-replacement decrease also observed in Denmark [Table 1].

Near-steady states are also possible in networks with low density [17], but the system does not fall back from a maximum. Owing to the fall from the maximum to changed environmental conditions by NPIs, seasonal effects, etc., raise the question of why activity in the system becomes stable rather than continuing to fall or rebound after another change in conditions. In the PMN model, this is the expected behavior.

|  |  |  |  |
| --- | --- | --- | --- |
| Fig 10  Cases in Italy 2022 | Fig 11  Cases in Denmark 2021 | Fig 12  Cases in Sweden 2021 | Fig 13  Cases in Italy 2020 |

### 4.2.3 Fading out of activity stimulated by temporary events

Mass gatherings are possible settings for considerable numbers of transmissions even though the time a case might spend in such an event is limited [2, 8, 13]. The EPNM conjecture does not imply anything particular for the transmissions at an event but has implications for the consequences: While a case originating in a transmission at a gathering will have the same number of random contacts as any other case—or there at least is no reason why not—the EPNM conjecture implies that, on average, there will be many immediate successor cases in a stable network but, as the environment outside the permeable networks does not support long transmission chains outside these networks, (almost) no distant successor cases. The EPNM conjecture thus implies a sharp rise shortly after the triggering event or after the event begins if it lasts for several days, followed by the fade-out of the additional stimulation a few virus generations thereafter.

The Munich Oktoberfest 2022, lasting from September 17th to October 3rd, is a particularly informative example of dynamics supporting the EPNM conjecture because the scenario was not obfuscated by changes in rules afterwards and because data can be compared with those of the rest of Germany [2, 15] [Table 2].

| Observable→ Period ↓ | **Munich: 7d incidence**  **(last day of week)** | **Bavaria:**  **7d incidence** | **Berlin:**  **7d incidence** | **Germany:**  **7d incidence** |
| --- | --- | --- | --- | --- |
| **Week 37 (09.12-09.18)** | 219 | 299 | 214 | 273 |
| **Week 38 (09.19-09.25)** | 395 | 406 | 230 | 341 |
| **Week 39 (09.26-10.02)** | 916 | 764 | 310 | 550 |
| **Week 40 (10.03-10.09)** | 1187 | 944 | 373 | 701 |
| **Week 41 (10.10-10.16)** | 947 | 895 | 468 | 772 |
|  | Peak in Munich, 10.12: 1550 – but reporting practice influences daily values | | | |
| **Week 42 (10.17-10.23)** | 357 | 596 | 451 | 649 |
| **Week 43 (10.24-10.30)** | 205 | 365 | 341 | 448 |
| **Week 44 (10.31-11.06)** | 109 | 201 | 233 | 291 |
| **Week 45 (11.07-11.13)** | 123 | 174 | 187 | 242 |
| **Week 46 (11.14-11.20)** | 92 | 122 | 161 | 201 |
| **Week 47 (11.21-11.27)** | 102 | 112 | 168 | 203 |
| **Week 48 (11.28-12.04)** | 107 | 112 | 239 | 220 |
| **Week 49 (12.05-12.18)** | 126 | 122 | 247 | 239 |
| **Week 50 (12.19-12.25)** | 150 | 127 | 291 | 266 |

Table 2 Cases in Munich before and during Oktoberfest and thereafter compared to Bavaria and Germany

There was a clear peak in Munich, as the 7-d incidence increased from 219 in week 37 to 1187 in week 40, whereas there was a much more moderate increase from 214 to 373 in Berlin and from 273 to 701 in Germany as a whole. Then, the number in Munich fell to 109 in week 44, where it became more or less stable, whereas that in Berlin fell to 233 in week 44. For the rest of the year, Berlin and Germany as a whole remained consistently higher than Munich and Bavaria as a whole. Considering that the numbers for Munich and Berlin were nearly identical in week 37 and that the numbers for Bavaria and Germany were also nearly identical, it appears that Oktoberfest exhausted parts of the pool of possible transmission paths. Together with rapid wild-type replacement, the fact that additional activity caused by transient events does not remain in the population is a strong argument for the EPNM conjecture.

### 4.2.4 Unpredictability of inflection points

As long as saturation effects in permeable networks do not matter much, models ignoring the modulation of the spread dynamics by PMNs will work well. However, they are unable to identify inflection points resulting from PMN saturation. This matches the observation that common models even late 2022, after nearly three years of fine-tuning, failed to make meaningful predictions [6] [Figures 14--16]. This is particularly significant since differences between predictions and reality in this case cannot be attributed to any type of NPIs or other unpredictable changes in environmental conditions.

|  |  |  |
| --- | --- | --- |
| Fig 14  Projections and real dynamics in France Oct-Nov 2022 | Fig 15  Projections and real dynamics, Germany Oct-Nov 2022 | Fig 16  Projections and real dynamics, Denmark Oct-Nov 2022 |

## 4.3 Concluding remarks

A formal construct has been presented that can be interpreted as a model of growth dynamics for a virus population or for two populations coupled by mutual inhibition. The model assumes that spread almost exclusively happens in contact networks and that the population of individuals in some of these networks changes over time at a rate implying an individual’s replacement probability in the range of 5%-50% for the virus infectious period. Additionally, the model allows the presence of two virus populations whose dynamics are coupled by mutual or asymmetric inhibition. In addition to permeable networks, the model assumes the existence of stable networks that support an index case’s transmission to multiple individuals in the stable network, whereas the environment outside the PNs does not support long transmission chains since random contacts connecting stable networks have a very low transmission probability.

The model generates processes of rapid replacement of a previous wild type by a more transmissible emergent strain, and it generates waves followed by a transition to near-steady states under constant environmental constraints. Similar patterns have also been reported in data concerning virus populations from the COVID-19 family.

An ultimate decision as to whether the formal construct of EPNMs is a plausible description of real-world events in the spread of Covid-19 strains or other viruses requires close examination of a sufficient set of genetically analyzed probes and comparison to the pattern of genetic similarities corresponding to the specific characteristics of the transmission graphs according to the EPNM conjecture. A final decision is impossible without such data and data analyses, but the match between available data and EPNM characteristics is noticeable.

# References

1. Bansal  Shweta,  Read Jonathan,  Pourbohloul Babak &  Meyers Lauren Ancel (2010)  [The dynamic nature of contact networks in infectious disease epidemiology, Journal of Biological Dynamics, 4:5, 478-489](https://www.tandfonline.com/doi/full/10.1080/17513758.2010.503376)

DOI: [10.1080/17513758.2010.503376](https://doi.org/10.1080/17513758.2010.503376)

1. [Berichterstattungen der Corona-Infektionszahlen in Bayern bis zum 01.06.23](https://www.lgl.bayern.de/gesundheit/infektionsschutz/infektionskrankheiten_a_z/coronavirus/karte_coronavirus/archiv2.htm). Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit
2. Beebeejaun K, Pebody R, Ciobanu S, Pukkila J, Smallwood C, Perehinets I. [UEFA Euro 2020: lessons from the first multi-city international mass gathering during the COVID-19 pandemic](https://pubmed.ncbi.nlm.nih.gov/36394345/). *Epidemiology and infection*. 2022;150:e182.

DOI :10.1017/S095026882200156X

1. Bhattacharya Alex, Collin Simon M, Stimson James, Thelwall Simon, Nsonwu Olisaeloka, Gerver Sarah, Robotham Julie, Wilcox Mark, Hopkins Susan, Hope Russell, [Healthcare-associated COVID-19 in England: A national data linkage study - ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0163445321004436) Journal of Infection, Volume 83, Issue 5, 2021, Pages 565--572, ISSN 0163--4453 <https://doi.org/10.1016/j.jinf.2021.08.039>

1. [European Centre for Disease Prevention and Control (2023) Archive](https://opendata.ecdc.europa.eu/covid19/virusvariant/xlsx/data.xlsx)

1. [European Covid-19 Forecats Modelling Hub](https://github.com/european-modelling-hubs/covid19-forecast-hub-europe_archive/tree/main/data-processed)
2. Günther, Thomas et al. [SARS-CoV-2 outbreak investigation in a German meat processing plant.](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7646008/) EMBO molecular medicine vol. 12,12 (2020): e13296.

doi:10.15252/emmm.202013296

1. Healthcare Denmark, [Pandemic response in Denmark – 2023](https://healthcaredenmark.dk/media/j3xcr1zb/3i-pandemic-response-pdf-uk.pdf) (2023)
2. Kim, Sungchan et al. [Evaluation of COVID-19 epidemic outbreak caused by temporal contact-increase in South Korea](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7224674/)  International journal of infectious diseases: IJID : official publication of the International Society for Infectious Diseases vol. 96 (2020): 454-457. doi:10.1016/j.ijid.2020.05.036
3. Komarova Natalia L., Azizi Asma, Wodarz Dominik, [Network models and the interpretation of prolonged infection plateaus in the COVID19 pandemic](https://www.sciencedirect.com/science/article/pii/S1755436521000220), Epidemics, Volume 35, 2021, 100463, ISSN 1755-4365, https://doi.org/10.1016/j.epidem.2021.100463.
4. Krall, P. (2021) [A network-based computational model showing responses to changing environmental constraints similar to patterns observed in the dynamics of the Covid-19 event](https://doi.org/10.20935/AL1581) Academia Letters, Article 1581, 2021, https://doi.org/10.20935/AL1581.
5. Krall, P. (2023) [Simulation of Rapid Wild-Type Replacement in Virus Populations](https://link.springer.com/chapter/10.1007/978-3-031-28076-4_33) In: Arai, K. (eds) Advances in Information and Communication. FICC 2023. Lecture Notes in Networks and Systems, vol 651. Springer, Cham. https://doi.org/10.1007/978-3-031-28076-4\_33
6. Oren Miron, Kun-Hsing Yu, [Outdoor mass gathering events and SARS-CoV-2 infection in Catalonia (North-East Spain)](https://www.sciencedirect.com/science/article/pii/S2666776222000436) The Lancet Regional Health - Europe, Volume 15, 2022, 100350, ISSN 2666-7762, <https://doi.org/10.1016/j.lanepe.2022.100350>.

1. [Our](https://ourworldindata.org/team) World in Data (2019-2023) [Coronavirus (Covid-19) Cases](https://ourworldindata.org/covid-cases)
2. Robert Koch Institut (2019-2023) [Wochenberichte zu COVID-19 (bis 8.6.2023)](https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Situationsberichte/Wochenbericht/Wochenberichte_Tab.html)
3. Rocha, L.E.C., Singh, V., Esch, M.  [Dynamic contact networks of patients and MRSA spread in hospitals](https://www.nature.com/articles/s41598-020-66270-9) Sci Rep 10, 9336 (2020). <https://doi.org/10.1038/s41598-020-66270-9>
4. Rosen, R. [Fundamentals of Measurement and Representation of Natural Systems](https://books.google.de/books?id=wnZQAAAAMAAJ), Elsevier, 1978.
5. Thurner, S., Klimek P., Hanel R. [A network-based explanation of why most COVID-19 infection curves are linear.](https://www.pnas.org/doi/10.1073/pnas.2010398117) Proc. Natl. Acad. Sci. U.S.A. 117, 22684–22689 (2020).
6. Tsori Y, Granek R (2021) [Epidemiological model for the inhomogeneous spatial spreading of COVID-19 and other diseases](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0246056). PLoS ONE 16(2): e0246056. https://doi.org/10.1371/journal. pone.0246056 Editor: Emanuele Giorgi, Lancast
7. Welcome Sanger Institute, [Sanger COVID–19 Genomic Surveillance](https://covid19.sanger.ac.uk/lineages/raw)