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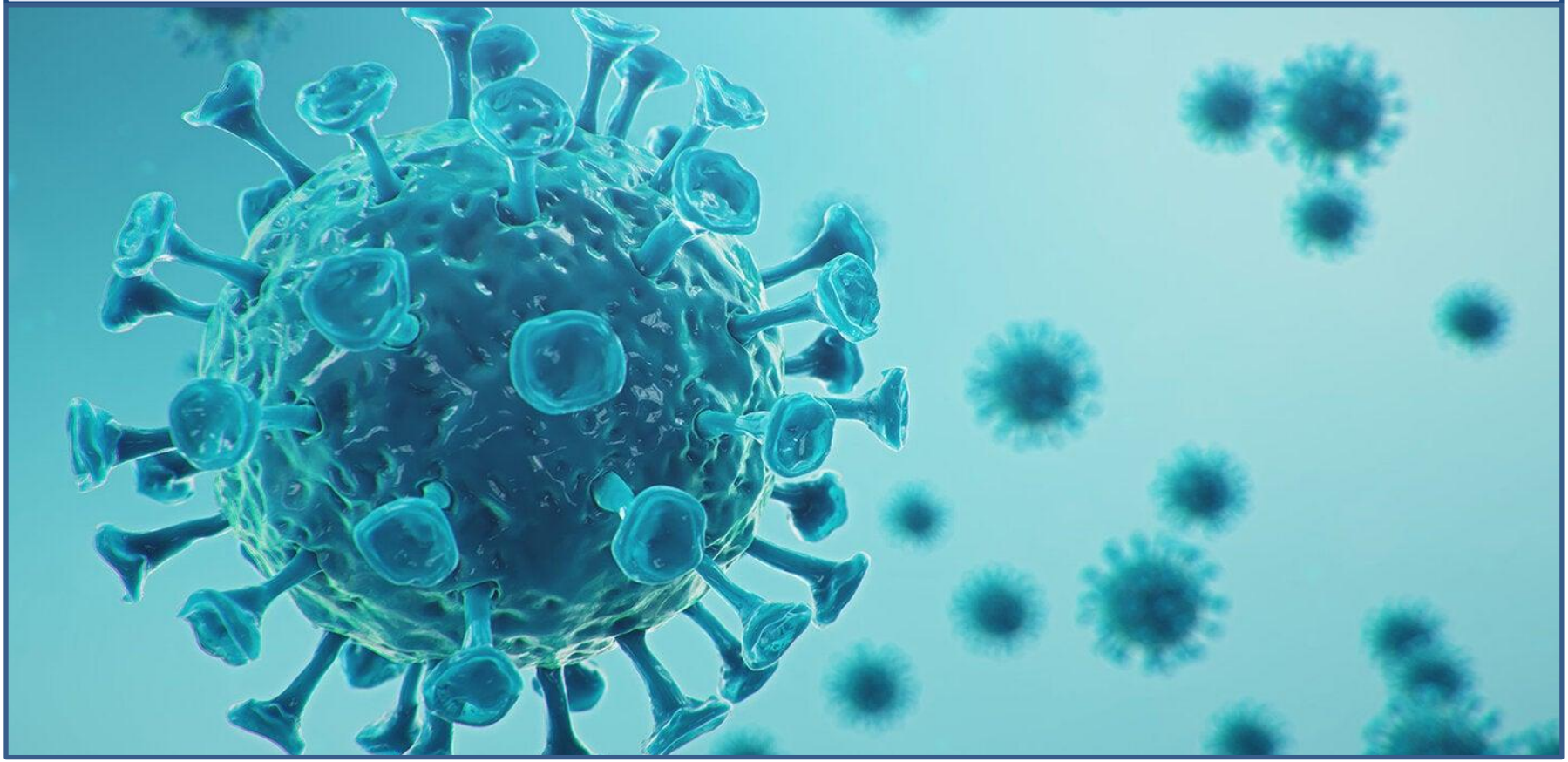
Studying the spread of epidemics using a spatial agent-based model and kinetic Monte Carlo simulations.



Since February 2020, hundreds, if not thousands, of scientific articles on modeling the spread of the COVID-19 pandemic have been published. Most studies used macroscopic ODE-type epidemiological models which are based on the mean-field approximation (MFA), such as the classic compartmental "Susceptible-Infected-Recovered" (SIR) model and its various modifications (SIS, SIRS, SEIR, SAIR, SIRD and others). A well-mixed population is assumed in these models. In general, relatively poor predictive power of SIR-type models was found.

Equations of the macroscopic SIR/SIRS model

$$\begin{cases} \dfrac{d\theta_I}{dt} = k_1\theta_I\theta_S - k_2\theta_I \\ \dfrac{d\theta_R}{dt} = k_2\theta_I - k_3\theta_R \\ \theta_S + \theta_I + \theta_R = 1 \end{cases}$$

θ_S – fraction of susceptible individuals (they can be infected)
θ_I – fraction of infected individuals
θ_R – fraction of recovered individuals

Initial conditions: $\theta_I(0)$, $\theta_R(0)$.

Parameters: k_1 – infection rate; k_2 – recovery rate; k_3 – immunity loss rate [time^{-1}]. Mortality is neglected.

When $k_3 > 0$, recovered individuals can become susceptible, it means that immunity can be lost after some time. When $k_3 = 0$, the SIRS model turns to the SIR model.

Advantage of the model – ease of use.

Drawback – the model neglects correlations in the location of infected and susceptible individuals, does not take into account their possible and impossible contacts; it is inherently assumed that any ill individual can infect any susceptible person (because of the term $k_1\theta_I\theta_S$).

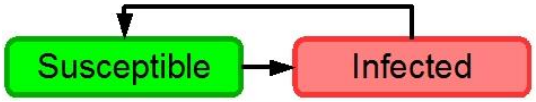
SIR-type epidemic model and some of its modifications

SIR

SIRS

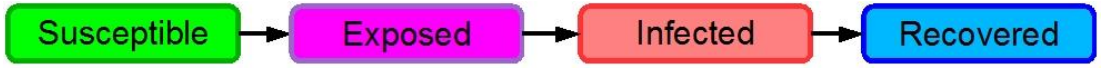
SIS

The simplest model



SEIR

A model for describing the spread of diseases with an incubation period.



MSEIR

SEIR + Maternally derived immunity.
Model takes into account the innate immunity of children.

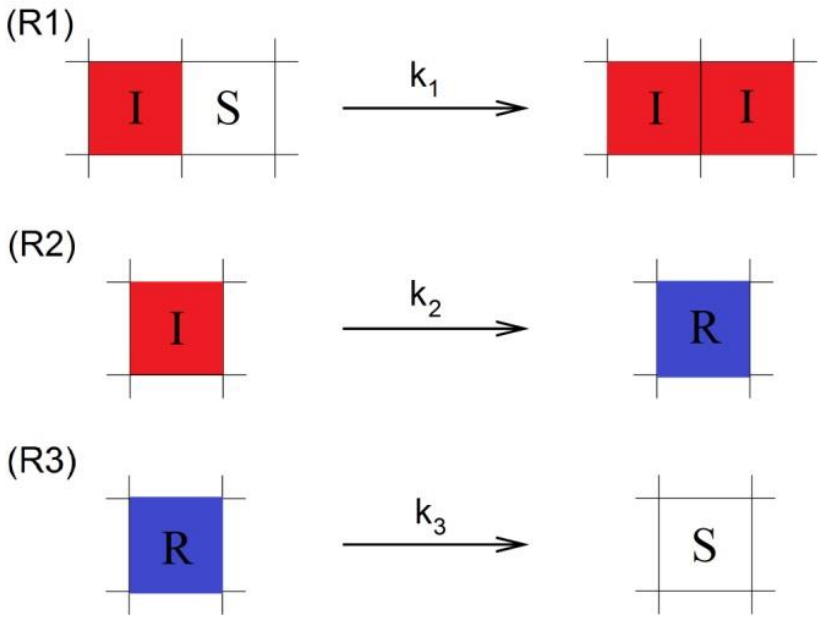
+ many others possibe models and states (e.g. dead, vaccinated, asymptomatic …)

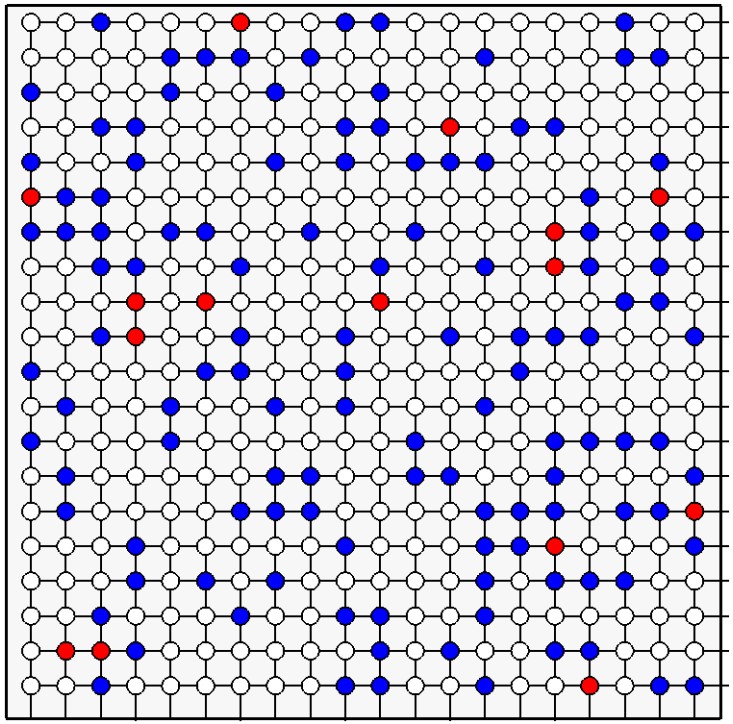
Our goal is to study a more complex spatial agent-based model that take into account limited contacts between infected and susceptible individuals, and explicitly describes their mobility (migration). Specifically, we consider the spatial agent-based epidemiological SIRS model using Kinetic Monte Carlo (KMC) simulations on a lattice.

Spatial individual-based model of the SIRS-type

Individuals are assumed to occupy the nodes on a regular square lattice. In a more general case, the possible contacts of individuals are given by the edges of a graph (network) on which the model is defined. Three possible states of nodes/individuals: **Infected**; **Recovered**, with immunity; **Susceptible**, healthy.

The main elementary events:





Lattice 20×20

- "**I**nfected
- **R**ecovered (immune)
- o **S**usceptible (healthy)

k_1, k_2, k_3 – transition rates (probabilities), [time^{-1}]

There are many different factors that influence the possibility of contacts between infected and susceptible people. For example, they are influenced by the quarantine measures carried out by the government. However, it is practically impossible to take into account all factors in the model.

Extended kinetic scheme for spatial "microscopic" SIRS model

We consider a regular square lattice containing N nodes. The possible elementary events (reactions):

$$(1)\quad I_i + S_j \xrightarrow{k_1} I_i + I_j \qquad (\text{infection})$$

$$(2)\quad I_i \xrightarrow{k_2} R_i \qquad (\text{recovery})$$

$$(3)\quad R_i \xrightarrow{k_3} S_i \qquad (\text{loss of immunity; } \textit{for SIRS only})$$

$$(4)\quad I_i + S_j \xrightarrow{d_1} S_i + I_j \qquad (\text{migration})$$

$$(5)\quad R_i + S_j \xrightarrow{d_2} S_i + R_j \qquad (\text{migration})$$

Five possible elementary events are considered that can occur with intensities k_1, k_2, k_3, $d = d_1 = d_2$. Stages (4) - (5) describe **the process of migration** by the exchange mechanism to the nearest neighboring nodes. The considered micromodel takes into account a limited number of contacts between people; for this, a lattice and the process of migration of individuals are introduced. This makes it possible **to single out one parameter (d)**, which determines the rate of mixing in the population and, thus, implicitly **takes into account all possible restrictive factors**. The case $d = 0$ corresponds to very strict quarantine measures. The case $d \to \infty$ corresponds to the SIRS macromodel and to completely random mixing, which cannot be realized in real life.

We use a spatial stochastic agent-based model, in which the system evolution is described by a Markov random process with a discrete set of states and continuous time, and the possible events are independent Poisson processes with given intensities.

The time variation of the probabilities of observation the possible discrete lattice states is described by the ***master equation***:

$$\frac{d\,\mathrm{P}_i(t)}{dt} = \sum_{j \neq i} \left(\mathrm{P}_j(t)\lambda_{ji}(t) - \mathrm{P}_i(t)\lambda_{ij}(t) \right), \qquad i = 1,2,\ldots,N_{eq}, \quad N_{eq} = 3^N$$

P_i – the probability of a state number i.

λ_{ij} – transition rate from state i to state j, [time^{-1}].

The assumption of random mixing, which is realized if $d \to \infty$, allows one to derive the SIRS macromodel from the master equation (at $N \to \infty$) or the Fokker-Planck equation for sufficiently large but finite sizes of the system N.

For the microscopic SIRS model on a lattice, the system contains 3^N linear first-order ODEs. It is impossible to solve such a system even when using small lattices. For example, for a 10×10 lattice, $N_{\mathrm{eq}} \approx 5.2\times10^{47}$. However, one can calculate sample trajectories of the system evolution using the kinetic Monte Carlo simulations. There are several statistically equivalent versions of the KMC method implementation. We use one of these methods which is called the “direct method” and refers to the “rejection-free” version of the algorithms.

Direct KMC method (rejection-free algorithm, Gillespie's algorithm for the lattice model)

Stage 1. *Initialization.*

Stage 2. *Calculation of the rates of elementary events.* At the current moment of time t, the velocities v_i of all possible events on the lattice, as well as the total rate V, are calculated.

Stage 3. *Determination of the moment when the system exits the current state.* The value of a random variable ξ_1, uniformly distributed over the interval $(0,1)$, is generated. The time spent by the system in the current state is calculated: $\Delta t = - \ln(\xi_1) / V$.

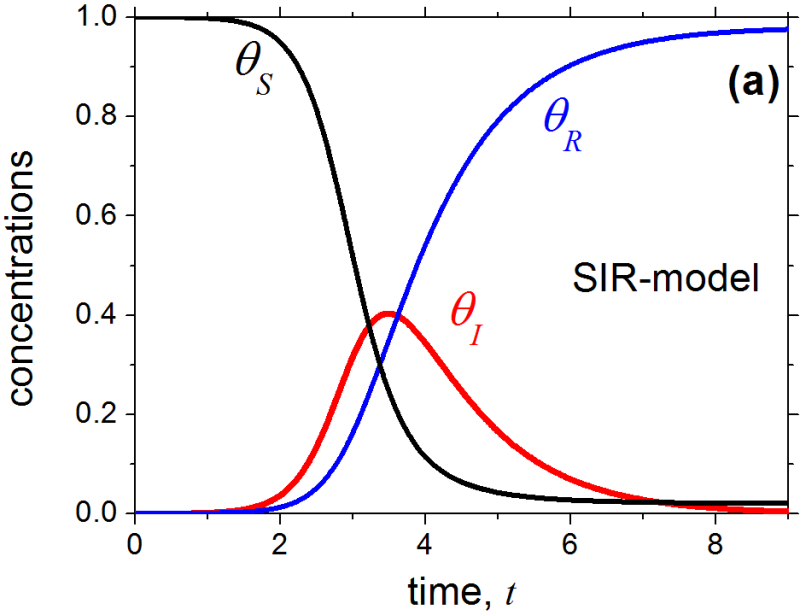
Stage 4. *Selection and implementation of an event.* One of all possible elementary events is chosen at random with a probability proportional to its rate. For this, a random real number $\xi_2 \in (0,1)$ is generated and a number p is determined such that

$$\sum_{j=1}^{p-1} v_j < \xi_2 V \le \sum_{j=1}^{p} v_j .$$

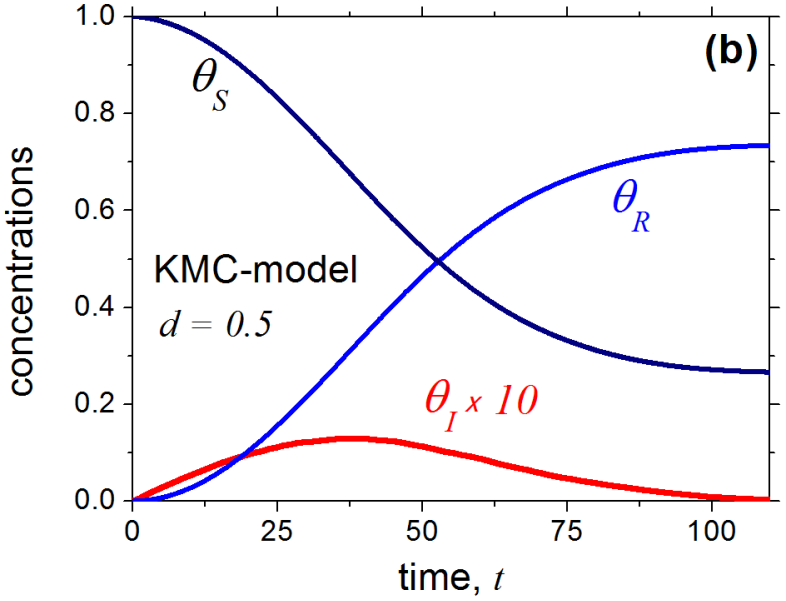
The selected p-th event is realized, the state of the lattice changes.

Stage 5. *Checking the criterion for the end of the simulation.* If the criterion is not met, then the transition to stage 2 is carried out with a new value of time $t = t + \Delta t$.

Let us compare the results of calculations using the standard SIR model and KMC simulations on a 5000 × 5000 lattice (with the same parameter values, but $d = 0.5$ for KMC).



SIR model

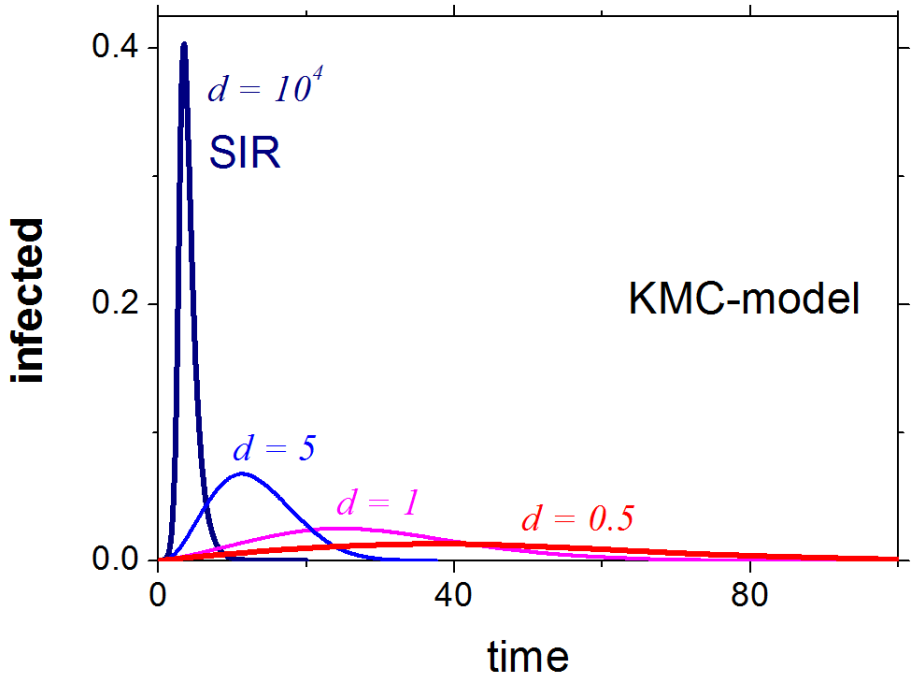


KMC simulations on a 5000×5000 lattice

Initial conditions: $\theta_I(0) = 10^{-4},\ \theta_R(0) = 0.$ Parameters: $k_1 = 1,\ k_2 = 1,\ k_3 = 0,\ d = 0.5.$

Compared with the KMC-model at $d = 0.5$, the SIR model reduces the characteristic epidemic time by approximately 10 times, but significantly increases the maximum number of simultaneously infected individuals (there are almost 30 times more of them), and increases the total number of recovered individuals ($\theta_R(t\to\infty)$).

KMC-simulations on a 5000×5000 lattice; influence of the migration rate on the results is shown



Initial conditions: $\theta_I(0) = 10^{-4},\ \theta_R(0) = 0.$

Parameters: $k_1 = 1,\ k_2 = 1,\ k_3 = 0$

The figure demonstrates significant differences between the simulation results for the fast and slow migration rates.

Conclusion: The widely used SIR model is too crude. A more realistic "microscopic" model, which takes into account the limited number of human contacts, predicts results that are very different from the predictions of the standard SIR macromodel. Slow migration can be a consequence of quarantine measures.

KMC simulations produce statistically exact sample paths of the Markov process under consideration, however, it is usually stated that this method is computationally very expensive. The simplest MFA assumes an infinite and well-mixed population. The pair approximation (PA) is an improvement over the MFA, it has been used many years ago in the studies of catalytic surface reactions. In the framework of a lattice-gas model, one can take into account not only a limited mobility of adsorbed particles, but also lateral interactions between them. It is known that PA can significantly improve the accuracy of calculations in comparison with MFA when the well-mixed hypothesis is not valid. However, PA also gives only an approximate solution of the original problem, and its computational accuracy is not controlled. For the lattice SIRS model, PA considers not only the concentrations of three types of individuals ($\theta_0 \equiv \theta_S$, $\theta_1 \equiv \theta_I$, $\theta_2 \equiv \theta_R$), but also the pair probabilities: $g_{i,j} = g_{j,i}$, where $i, j = 0, 1, 2$. On an infinite square lattice, the **PA-model equations** can be written as:

$$\frac{d\theta_1}{dt} = 4k_1 g_{1,0} - k_2\theta_1, \qquad \frac{d\theta_2}{dt} = k_2\theta_1 - k_3\theta_2,$$

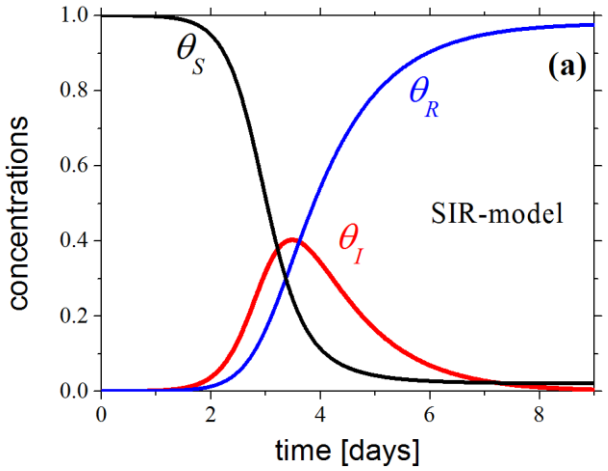
$$\frac{dg_{1,1}}{dt} = 2k_1 g_{1,0} + 6k_1 g_{1,0}\varphi_{0,1} - 2k_2 g_{1,1} + 6d_1 g_{1,0}(\varphi_{0,1} - \varphi_{1,1}),$$

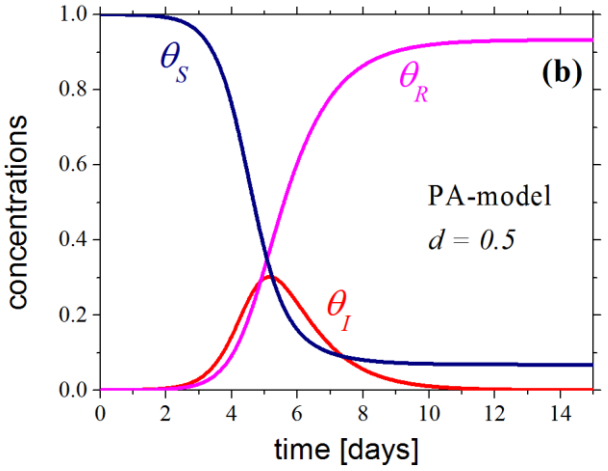
$$\frac{dg_{1,2}}{dt} = 3k_1 g_{1,0}\varphi_{0,2} + k_2(g_{1,1} - g_{1,2}) - k_3 g_{1,2} + 3d_1 g_{1,0}(\varphi_{0,2} - \varphi_{1,2}) + 3d_2 g_{2,0}(\varphi_{0,1} - \varphi_{2,1}),$$

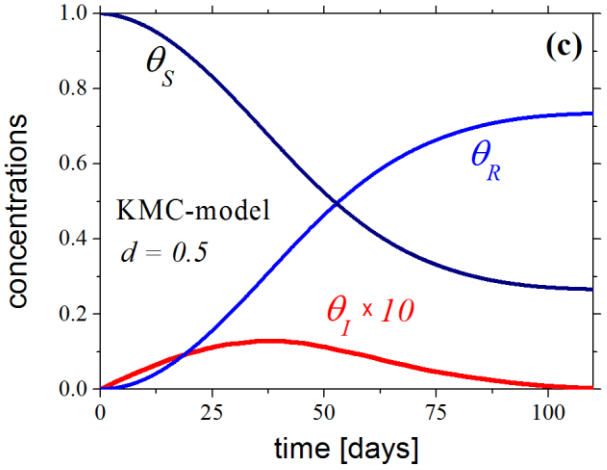
$$\frac{dg_{2,2}}{dt} = 2k_2 g_{1,2} - 2k_3 g_{2,2} + 6d_2 g_{2,0}(\varphi_{0,2} - \varphi_{2,2}),$$

where $\varphi_{i,j} = g_{i,j}/\theta_i$. Conservation laws provide additional conditions: $\theta_i = g_{i,0} + g_{i,1} + g_{i,2}$.
The standard SIRS model is derived from the PA-model if $d_1 \to \infty$ and $d_2 \to \infty$. In this case, $g_{ij} = \theta_i\theta_j$ (for all $i, j = 0,1,2$).

Let us compare the results of calculations using the standard SIR model, PA model and KMC modeling on a 5000 × 5000 lattice with the same parameter values ($d = 0.5$ for PA and KMC).





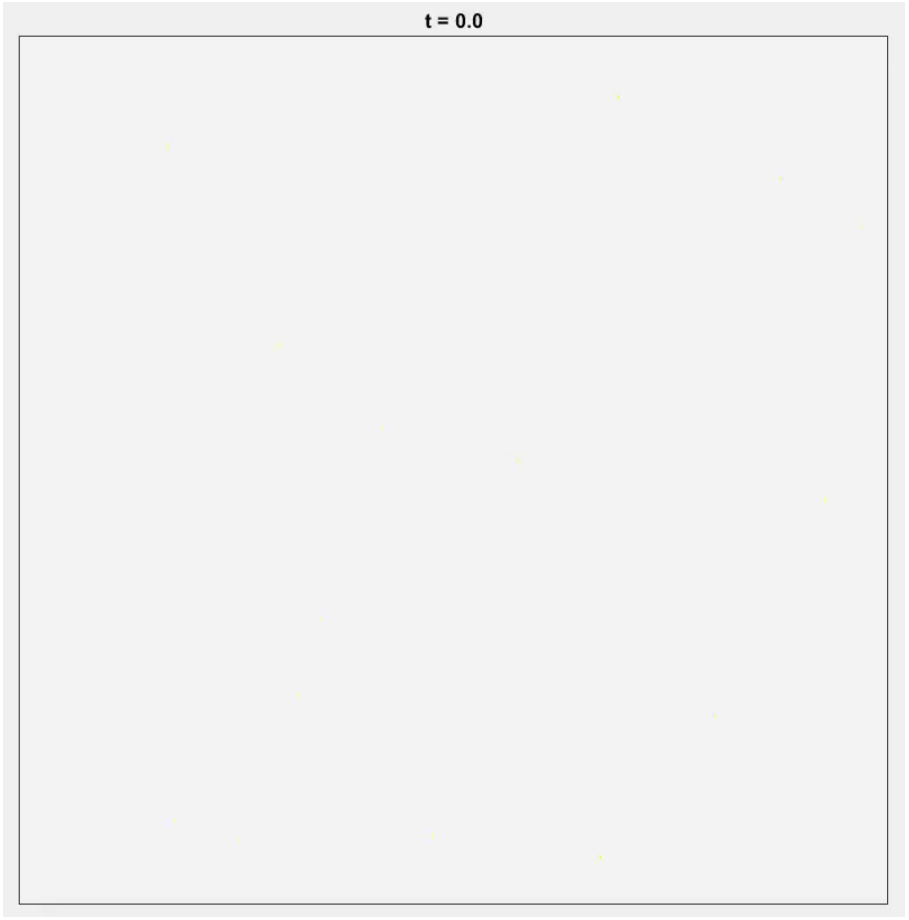


$\theta_I(0) = 10^{-4},\ \theta_R(0) = 0.\quad k_1 = 1,\ k_2 = 1,\ k_3 = 0,\ d = 0.5.$

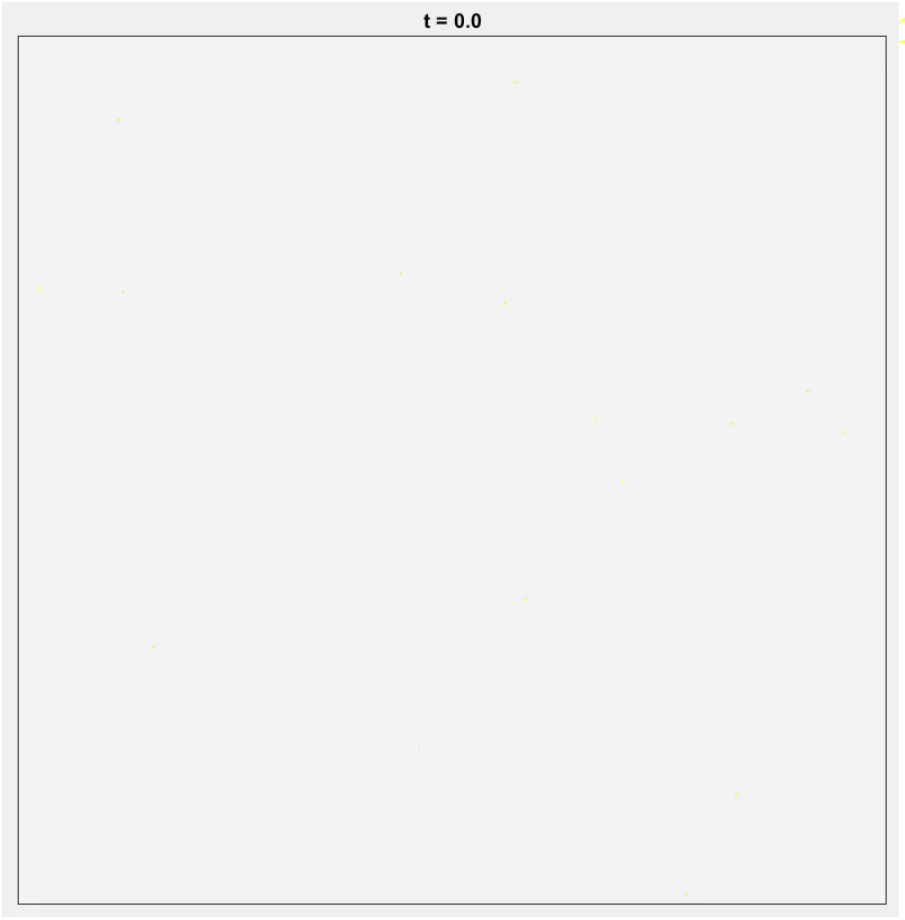
We see that the PA model gives the results which better describes the KMC simulations than the SIR model, however, the accuracy of PA is also very low. For example, the characteristic time of the epidemic in the PA model is about 7 times smaller than that in the KMC model.

The PA model is also crude, although it is better than standard SIR!

SIR; KMC-simulation on a 400×400 lattice.



$d = 100$



$d = 0.5$

Initial conditions: $\theta_I(0) = 10^{-4},\ \theta_R(0) = 0$

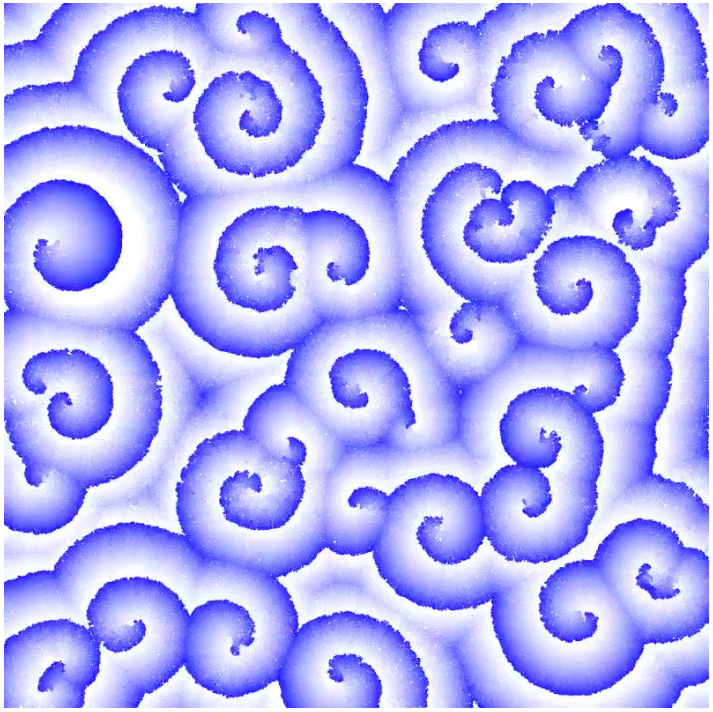
Parameters: $k_1 = 1,\ k_2 = 1,\ k_3 = 0$

• Infected; • Recovered; o "Susceptible

The films show significant differences between the simulation results at fast and slow migration rates. The characteristic time of the processes differs by a factor of ≈10, the number of infected individuals and their spatial distribution are also very different.

SIRS; KMC-simulation on the 20000×20000 lattice (400 mln people)

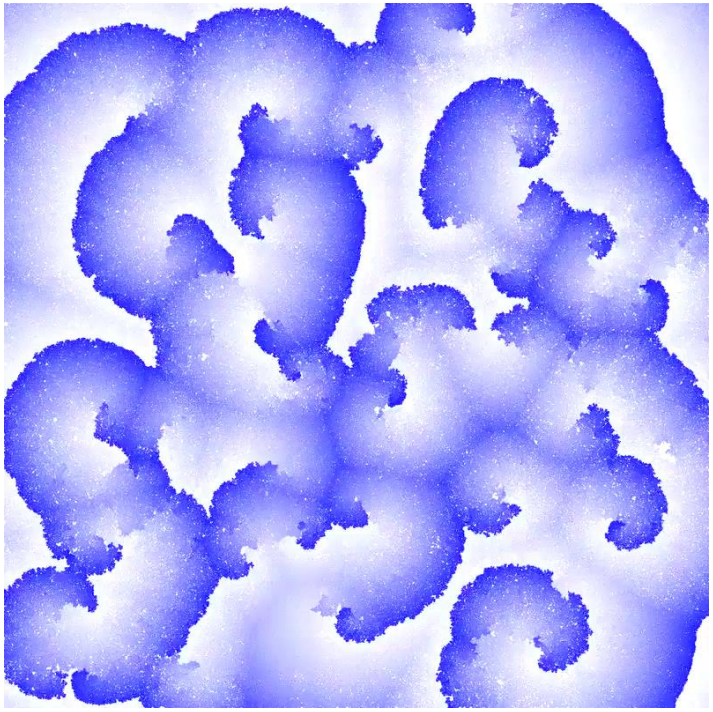
The condition $k_3 > 0$ means that people who have recovered will lose their immunity over time. In this case, the SIRS lattice model represents an excitable medium. The films show a state of the system called “spiral chaos”. Fragments of spiral waves are observed that rotate, collide, partially annihilate, create new fragments. The blue color shows those people who have been ill and have immunity (≈ 50% of the population). People susceptible to the disease correspond to white color (they are also ≈50%). Infected individuals are not visible as their concentration is only about 0.05%. They form the epidemiological wave fronts, which can spread only to areas where there are many susceptible people (waves "infect" light areas).



$k_3 = 0.005;\ \theta_I(t) \approx 0.0027,\ \theta_R(t) \approx 0.53$

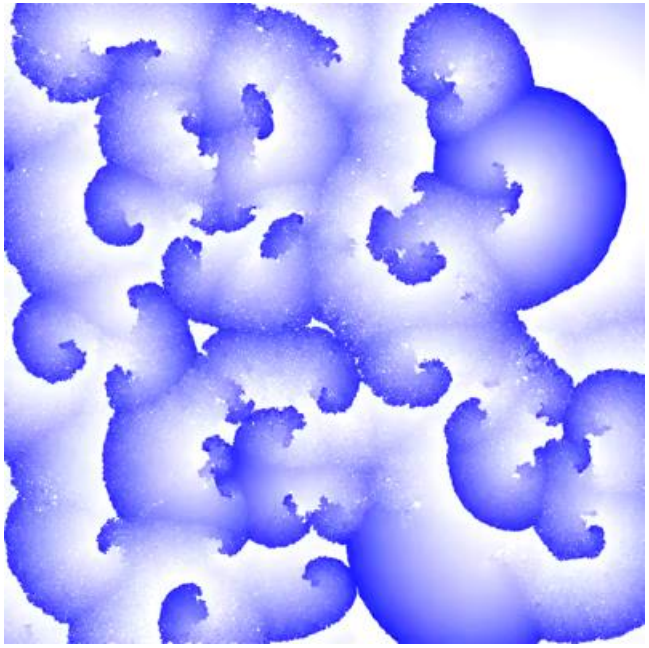
Parameters:

$k_1 = 5,\ k_2 = 1,\ d = 0$



$k_3 = 0.001;\ \theta_I(t) \approx 0.0005,\ \theta_R(t) \approx 0.525$

SIRS; KMC-simulation on the 40000×40000 lattice (1.6 billion people)



Parameters: $k_1 = 5,\ k_2 = 1,\ k_3 = 0.001,\ d = 0$

$\theta_I(t) \approx 0.0005,\ \theta_R(t) \approx 0.525$

The SIRS macromodel assumes a spatially homogeneous state of the system. The micromodel shows the virus circulation in the form of spiral waves, the characteristic rotation period of which is ~2 years. The state of spiral chaos can be observed for an arbitrarily long time. This pattern is observed due to the fact that after a long time, immunity disappears in individuals who have had a viral infection. Therefore, the virus persists in the population, despite the small number of simultaneously ill individuals (in this case, about 800 thousand people out of 1.6 billion of the population are simultaneously sick). Only vaccination of the population can help to avoid such space-time chaos. If the population is not vaccinated, then conditions are created for an eternal pandemic.

Simulations can be used to estimate the number of vaccinations needed to stop the virus from circulating. For the conditions under consideration, which correspond to very stringent restrictive measures, it is necessary to vaccinate only ≈20% of the population in order to completely stop the spread of the virus.

The epidemiological model we have considered uses a regular two-dimensional lattice as a network and assumes uniformity of parameters for all individuals, which significantly simplifies calculations. Further work can be directed towards building more complex network models, which take into account the heterogeneity of different groups and the variable/adaptive structure of the network. Building realistic networked agent-based models is an interesting and practically meaningful task (e.g., in bio-medical and socio-economic problems).