# A Discrete SIR Model with Spatial Distribution on a Torus for COVID-19 Analysis using Local Neighborhood Properties

Reinhard Schuster<sup>1</sup>, Klaus-Peter Thiele<sup>2</sup>, Thomas Ostermann<sup>3</sup> and Martin Schuster<sup>4</sup>

<sup>1</sup>Chair of Department of Health Economics, Epidemiology and Medical Informatics, Medical Advisory Board of Statutory Health Insurance in Northern Germany (MDK Nord), 23554 Lübeck, Germany

<sup>2</sup>Medical Director of the Medical Advisory Service Institution of the Statutory Health Insurance in North Rhine (MDK Nordrhein), 40212 Düsseldorf, Germany

<sup>3</sup>Chair of Research Methodology and Statistics in Psychology, Witten/Herdecke University, Alfred-Herrhausen-Straße 50,

58448 Witten, Germany

<sup>4</sup>Faculty of Epidemiology, Christian-Albrechts University Kiel, 24105 Kiel, Germany

Keywords: COVID-19, SIR Model, Torus, Differential Equation, Laplace Operator, Mean Value Operator.

Abstract: The ongoing COVID-19 pandemic threatens the health of humans, causes great economic losses and may disturb the stability of the societies. Mathematical models can be used to understand aspects of the dynamics of epidemics and to increase the chances of control strategies. We propose a SIR graph network model, in which each node represents an individual and the edges represent contacts between individuals. For this purpose, we use the healthy S (susceptible) population without immune behavior, two I-compartments (infectious) and two R-compartments (recovered) as a SIR model. The time steps can be interpreted as days and the spatial spread (limited in distance for a singe step) shell take place on a 200 by 200 torus, which should simulate 40 thousand individuals. The disease propagation form S to the I-compartment should be possible on a k by k square (k=5 in order to be in small world network) with different time periods and strength of propagation probability in the two I compartments. After the infection, an immunity of different lengths is to be modeled in the two R compartments. The incoming constants should be chosen so that realistic scenarios can arise. With a random distribution and a low case number of diseases at the beginning of the simulation, almost periodic patterns similar to diffusion processes can arise over the years. Mean value operators and the Laplace operator on the torus and its eigenfunctions and eigenvalues are relevant reference points. The torus with five compartments is well suited for visualization. Realistic neighborhood relationships can be viewed with a inhomogeneous graph theoretic approach, but they are more difficult to visualize. Superspreaders naturally arise in inhomogeneous graphs: there are different numbers of edges adjacent to the nodes and should therefore be examined in an inhomogeneous graph theoretical model. The expected effect of corona control strategies can be evaluated by comparing the results with various constants used in simulations. The decisive benefit of the models results from the long-term observation of the consequences of the assumptions made, which can differ significantly from the primarily expected effects, as is already known from classic predator-prey models.

### **1 INTRODUCTION**

The Covid-19 pandemic is a major challenge for physicians, politicians, scientists and much other groups. Models are useful to discuss possible scenarios and implications of interventions to expand background knowledge and to design policy impact research, cf. (Chinazzi et al., 2020), (Rosenbaum, 2020), (Pan et al., 2020), (Behrens et al., 2020), (Tang et al., 2020).

The contextual selection of adequate models

should be able to generate all known actual and historic observations by choosing suitable model classes and parameters, cf. (Bailey, 1975), (Keener and Sneyd, 1998), (Xue et al., 2020), (Kucharski et al., 2020). As an intermediate step, the advantages and disadvantages of known mathematical models in medicine and biology and their implementations in informatics using different classes of parameters should be analyzed, cf. (Kermack and McKendrick, 1933).

The biomathematical analysis of epidemiological systems has a long history, cf. (Arnautu et al., 1989),

DOI: 10.5220/0010252504750482

In Proceedings of the 14th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2021) - Volume 5: HEALTHINF, pages 475-482 ISBN: 978-989-758-490-9

Copyright © 2021 by SCITEPRESS - Science and Technology Publications, Lda. All rights reserved

Schuster, R., Thiele, K., Ostermann, T. and Schuster, M

A Discrete SIR Model with Spatial Distribution on a Torus for COVID-19 Analysis using Local Neighborhood Properties.

(Aronson, 1985), (Beretta and Capasso, 1986). The family of SIR models with various generalizations of the status elements S (susceptible), I (infected or infectious) and R (removed or recovered) with respect to other status elements as E (exposed) and subpopulations use ordinary differential equations, cf. (Ahmed and Agiza, 1998), (Andersen and May, 1979), (Capasso, 1993), (Redheffer and Walter, 1984).

The variables are fractions of the population modelled as positive real numbers as in the mass action law supposing homogeneous distributions. Periodic solutions of first order ordinary differential equations are unstable with respect to system parameters. A large number of SIR models use bilinear differential equations, cf.(Rüdiger et al., 2020).

We propose a model which could be presented as a cellular automata. In order to use methods of partial differential equations and mean value operators in differential geometry we use differential manifolds as a general modelling background and its discretization which generalizes the Euclidean structure of cellular automata, cf. (Mikeler et al., 2005), (Günther and Prüfer, 1999), (Schuster, 1988), (Schuster, 1997), (Wang et al., 2015), (Welch et al., 2011).

An essential feature will be the visualization of development of the pandemic with special structures, cf. (Murray, 2002), (Murray, 2003), (Barrat and Vespignani, 2008), (Andersen and May, 1979). This will be realized with Mathematica from Wolfram Research which also allows to use a syntax without coordinates. A visualization of the pandemic status of 40 thousand individual can be reached with some hours of calculation time. The results to be considered in the following have proven to be the optimal solution within the used simulations with regard to the target variable that is still to be discussed.

If one would change the discretization of the torus structure of the used differential manifold by a graph structure (cf. (Solimano and Bretta, 1982), (Rüdiger et al., 2020), (Welch et al., 2011), (Boguna et al., 2003)) much less individuals could be visualized.

Cyclical structures in the sense of a boundary cycle or a cyclical band were discussed in chemical and biological examples, where there are fundamental theoretical differences, but also commonalities between discrete and continuous systems, cf. (Capasso and Maddalena, 1983), (Field and Burger, 1985). When modeling exponential growth, there are not only differences between continuous and discrete systems, but also between spatially bounded and unbounded systems (compact and non-compact manifolds in differential geometry), cf. (Murray, 2002), (Murray, 2003), (Barrat and Vespignani, 2008), (Beretta and Capasso, 1986), (Boguna et al., 2003), (Solimano and Bretta, 1982). In this context, the r-value plays a role in the current Covid-19 discussion that has already been analyzed earlier in various contexts, cf. (Dieckman et al., 1990). The r-value should describe the prevailing value of an exponential spread. The exponential mapping provides the crucial relationship between Lie algebras and Lie groups in differential geometry. This goes far beyond the exponential function on real numbers, which already shows a completely different qualitative behavior on complex numbers. Using the exponential function to describe the spread of Covid-19, which could practically never be sensibly modeled with an exponential spread, leads to theoretical and practical problems. The exponential map on a discretized torus leads to a growth in which the saturation value has to be estimated, which is in principle impossible from short initial data. The actual paper is a first step in the stated context.

## 2 MATERIAL AND METHODS

Individuals are the elements of an *n* by *m* array (in the examples we use the special values n = m = 200). Individuals can be in the status *S* (susceptible: healthy without immune behavior),  $I_1$  or  $I_2$ (infected or infectious after incubation period) and  $R_1$  or  $R_2$  (recovered with immune behavior) for each day after initialization. Further on for every individual in the  $I_1$ ,  $I_2$ ,  $R_1$  or  $R_2$  status the number of days being in that status is considered, cf. Figure 1. It is also possible to model different immune behavior specifically related to the infectious disease in different S compartments, here this is be done in the R compartments.

The right and left hand as well as the upper and lower elements of the array resulting from the discretization of the torus are connected. If one would change the upper and lower side of the right and left sides of the array and respectively for the upper and lower side we would get the discretization of double Möbius strip which can't be realized in three dimensional geometry. With an other boundary identification one also could reach the topology of a sphere.

As a local neighborhood of the array element (i, j) we consider all elements  $(i + k, j + k) \mod n$  with  $-m \le k \le m$  (m = 5 in the examples). An *S* individul in the local neighborhood of a *I* individual is infected randomly with equal probability with the property that during the infectious period *r* individuals (*r* as the theoretical reproduction number) are infected. This theoretical reproduction number supposes that all other individuals in the local neighborhood are in the *S* status.

The individuals of the  $I_2$  compartment are less in-



Figure 1: SIR compartments and transitions p.

fectious than those of the  $I_1$  compartment but over a longer period of time, both lead to the same resulting reproduction number in the used simulation. This assumption can be modified.

The individuals of the  $R_2$  compartment should be immune longer than those individual of the  $R_1$  compartment. At the beginning of the simulation, all individuals should belong to the S compartment with the exception of  $i_1$  and  $i_2$  individuals, respectively, randomly determined individuals of the  $I_1$  and  $I_2$  compartments. The previous time in the  $I_1$  or  $I_2$  compartment should also be chosen randomly. This means that at the beginning of the observation of the spread there is no immune behavior. With regard to measures to be taken to limit the spread of the infection, this is the most unfavorable option. Alternatively, one could start with an initial distribution of individuals in  $R_1$ and  $R_2$  compartments. Since simulations have shown that the same dynamic behavior will occur in the medium term, it was easier to choose comparable initial conditions.

After the infectious period of individuals of  $I_1$  or  $I_2$  they change to  $R_1$  or  $R_2$  individuals by transition parameters. After immunity, the individuals switch back to the S compartment. There also may be a switch between  $I_1$  and  $I_2$  individuals. The transitions  $p_i$  (i=1,...10) between the compartments are shown in Figure 1. In the considered context the  $p_i$  are stochastic processes depending on the previous length of stay of the individuals of the compartments. In an analog Markov model, these are only transition probabilities.

The daily steps are simultaneously using the previous day's conditions for all transitions. This includes that an individual in an R-compartment which changes to the S-compartment can not change from another individual to an S-compartment through infection during this step. In this way, an overall effect of all other individuals in the local contagious neighborhood is achieved.

*S* individuals may be infected by all  $I_1$  or  $I_2$  individuals in the related local neighborhood with resulting increasing probability with the number of these individuals, similar to a bilinear infection in SIR models without spacial structure. Thereby the new  $I_1$  or  $I_2$  individuals are determined. After that step  $R_1$  or  $R_2$  individuals may switch to *S* individuals and  $I_1$  or  $I_2$  individuals may switch to  $R_1$  or  $R_2$  individuals. The parameters of the simulation should be determined in such a way that

- 1. the  $I_1$  compartment is as small as possible
- 2. the transition probability from the *S* compartment to the  $I_2$  compartment (long infectious) is smaller than that into the  $I_1$  compartment (short infectious) and
- 3. a large proportion of the population reaches the  $R_1$  or  $R_2$  compartment.

Small *I* compartments and large *R* compartments are opposing objectives, since only *I* individuals can become *R* individuals.  $I_1$  individuals can be interpreted as symptomatic cases or as individuals with stronger disease symptoms and  $I_2$  individuals as asymptomatic cases or with lower disease symptoms. We want to reach large immunity with low treatment cases as a target. The system should be able to generate approximately stable cyclical behavior (including a cyclic band with chaotic behavior in the inner band part), because states of equilibrium can be unstable possibly solely through external influences.

Of central interest is how the system settles. If the first or second oscillation (first or second wave) is significantly higher than later oscillations of small amplitude for the diseases, a new infection from outside is a high risk as immunity declines. A small regular rate of contamination from outside should realistically be included in the model.

The approach considered is a discretization of a partial integro-differential equation with an additional time delay. The effect of the local environment can be viewed as a mean value operator. It is known from differential geometry that the eigenvalues of the Laplace operator are also eigenvalues of the mean value operators and that eigenfunctions of the mean value operators and can be calculated from those of the Laplace operator, with no time delays being included in the considerations of differential geometry. Instead of the time delays, as is usual in SIR models, transition probabilities can be replaced, which can be modeled as reciprocal values of the expected value of remaining time in the compartment.

## **3 RESULTS**

We start with 10 randomly infected individuals of the I population, all other individuals should initially be in the S compartment. This number is important with regard to the number of initial clusters of the infection and should initially model a low external influence. A small number extends the initial phase, a high number induces a dynamic that has to be synchronized with an approximately periodically stable internal system dynamic. Half of the individuals in the I compartment should initially be in the  $I_1$  compartment, the other in the  $I_2$  compartment. An incubation period is not included in the results considered here, but in the previous simulations they have not led to any other qualitative results. These only show changes in the initial phase of the development of the infection.

The results of this section are calculated with the optimal parameters with respect to the mentioned goal to reach low infections over the time including the initial phase and a large number of immune individuals over the time out of over 100 long time simulations. In addition to the spatial distributions and progress figures in the individual compartments, we will provide qualitative comparisons with the other simulations carried out.

Individuals in the  $I_1$  compartment should be contagious for two weeks, and individuals in the  $I_2$  compartment for 10 weeks, this is a ratio of 5. Other ratios have shown less stable results or worse results in relation to the main target.

Due to the large number of incoming parameters, the search for an optimum was only able to find a locally optimal version. Further theoretical analyzes are necessary at this point.

The time unit primarily used is also to be regarded as provisional. The need for an adjustment may arise from the cycle durations resulting from the long-term behavior.

The r-value of the RKI (Robert Koch institute) often used in Germany results from ratios of two latest available consecutive three day incidence numbers. If the used time step is shorter than a day the r-value becomes more stable.

Every individual of the  $I_1$  population shall have a theoretical (initial) r-value of 3. This shall men, that this individual would infect 3 other individuals throughout his infection period, if all individuals in the considered local neighborhood under consideration belonged to the S compartment. Half of the newly infected individuals should get into the  $I_1$  and  $I_2$  compartments.

One could assume that smaller theoretical initial r-values would be desirable. As a result of the mo-

re slowly developing immunity, however, they lead to more diseases in the initial phase and to higher longterm stability with repeated high numbers of diseases. High initial r-values lead to high values in the  $I_1$  compartment, with an interpretation that leads to high case numbers in hospital care and should therefore be avoided as a priority. The proportion of hospital cases within the  $I_1$  compartment is not considered here, as it has at most a marginal effect on the spread dynamics.

Individuals in the  $I_2$  compartment should only be 5% as contagious as individuals in the  $I_1$  compartment, with half of the new infections reaching the  $I_1$ and  $I_2$  compartments. But this  $I_2$  compartment has a major influence on the dynamics of the spread, as the longer residence time in this compartment has a stabilizing effect on the spatial distribution of the compartments. If dynamic differences between the  $I_1$  and  $I_2$  compartments are too small, there is no spatial stabilization effect. If the differences are too large, the overall effect of the  $I_2$  compartment is too small. In between there is at least a local optimum with regard to the central target variable with regard to the ratio considered here.

In addition, there should be an external possibility of infection. Complete isolation of a region is an illusion, especially with regard to asymptotic cases, and would only lead back to the unfavorable settling phase.

Every fifth day a randomly selected individual is infected if this is in the S compartment. This results in a slight acceleration in the initial phase of the dynamics of the epidemic and has almost no effect if the immune behavior is widespread. This approach prevents the infection from escalating under the illusion that a region can be completely isolated from the outside world.



Figure 2: S-I-R compartments at day 91, 182, 273 and 365 (from top left to bottom right).

After the contagion phase, 90% of the individuals in the  $I_1$  compartment should be randomly selected to move to the  $R_1$  compartment, the rest to the  $R_2$  compartment. Based on the  $I_2$  compartment, it should be 80% respectively. A thoroughly interesting interaction between the  $I_1$  and  $I_2$  compartments is initially not considered here, since this results in a strong interaction with regard to a meaningful determination of the parameters to be used and significantly extends the search process for meaningful combinations. The individuals in the  $R_1$  compartment should remain there for 180 days (about half a year), those in the  $R_2$  compartment for three times that time. With these parameters, after one quarter (91 days), the division into the S-I-R compartments is shown in Figure 2 top left. The colors are those used in Figure 1. The S compartment with value 1 is shown in yellow. The  $I_1$  compartment is shown in lighter red (value 2) and  $I_2$  in darker red (value 3). Intuitively, red should act as a warning color according to the traffic light symbols. The temporarily immune compartment is shown in green, the lighter green (value 4) with shorter immunity than the darker green (value 5).

The specified r-value in the figure is the value used by the RKI (Robert-Koch Institute in Germany), which describes the ratio of new infections from two consecutive 3-day periods. If you follow the results in detail, you can quickly see that this value describes the development of the infection very poorly and misleadingly in the used simulation.

The epidemiological situation of the next quarter (day 182) is described in Figure 2 top right.

In this simulation, over 75% of the population is not yet affected by the epidemic. It can be seen to a large extent through the strong creative power of random processes caused the emergence of distribution patterns. Pattern creation has been discussed in mathematical modeling in chemical, biological and medical applications for many decades, especially in the case of diffusion effects, and is relevant to the approach considered here, cf. (Murray, 2002), (Murray, 2003), (Aronson, 1985), (Capasso and Maddalena, 1983). The Laplace operator already discussed plays a decisive role in diffusion processes. Spectral results (eigenvalues and eigenvectors) of the Laplace operator are relevant for pattern formation.

Regarding the strong design ability of random processes, it should be noted that with random primes it was possible to depict properties of prime numbers as motivated, the proof of which has not been successful for hundreds of years. Why this is so is largely unclear and is a challenge for future research. These considerations are not based on simulations, but on calculations using the stochastic approach. Such an approach is also useful for the present topic.

The epidemiological situation of the next quarter (day 273) is described in Figure 2 bottom left.

About half of the population is affected by the epidemic. The pattern emergence is largely shaped by the previous quarter. One year after the start of the simulation, a high level of immunity is achieved, although this is associated with few new infections.

Before details of the next few years are presented, the time series in the compartments should be considered in Figure 3. After a large initial swing, the Scompartment stabilizes at approx. 75% of the population with a variation of approx. 25% of the population in the considered simulation.

As shown in Figure 3 the  $I_2$  compartment shows significantly lower amplitudes than the  $I_1$  compartment.



Figure 3: Time series of the *S* compartment (top left),  $I_2$  compartment (top right),  $R_1$  compartment (bottom left) and  $R_2$  compartment (bottom right).



While the  $I_1$  and  $I_2$  compartments show a high degree of correspondence over time, there are significant qualitative differences for the  $R_1$  and  $R_2$  compartments.

After some years, the epidemic system is still in the settling phase.

In the years nine and ten after the start of the simu-



Figure 5: S-I-R compartments after 2, 3 9 and 10 years (from top left to bottom right).

lation, the epidemic essentially shows the long-term dynamics.

If the time step is really shorter than one day, then the number of years for the settling process is correspondingly shorter. For long-term observations, annual influences on the assumed constants of infection are relevant. This process of synchronization between the internal clock and the external clock has long been discussed in the biomathematical literature and will be taken up in a later paper.

## 4 DISCUSSION AND CONCLUSIONS

The dynamics of the development of the epidemic is influenced by the interaction of all parameters used. Only then does it become apparent whether the time unit used is compatible with the observation. The results suggest that the time unit used is significantly shorter than a day and thus the observation period is shorter than ten years. This implies that the given RKI r-value becomes more stable without its fundamental problem changing. The r-value varies at relatively short intervals between values below and above 1. The simulations show that it has no significance for the formation of new regional clusters. Regional clusters can trigger regional interventions with a suitable scaling, which, however, as already mentioned, can be counterproductive to the development of immune behavior. To make matters worse, only the  $I_1$  compartment is visible, but the dynamics are essentially determined by the entire I compartment. This naturally also raises the question of whether the r-value (real and in the simulation) should be calculated with the entire *I* compartment or only with the  $I_1$  compartment. The entire *I* compartment is useful for the simulation, but only the  $I_1$  compartment is practically measurable. A further complication arises because there are no representative estimated values for the population, but Covid-19 test results are only available through measures that are essentially politically selective. Tracking Covid-19 contact chains with extensive quarantine can limit the positive development of immunity by the  $I_2$  population. Since this happens predominantly, only selectively, it will only lead to a few spatial disparities that are already present through pattern creation processes.

Infectious diseases often vary from season to season. This can be implemented in the model in that the transition probability used are subject to a seasonal course. However, this only makes sense if the time unit resulting from the combination of the parameters used has been adapted sufficiently reliably to real time units. The synchronization of different time scales poses is a challenge for future research. The modeling on the torus could be extended by bifurcation at certain points or intervals, which leads to a directed graph in the graph-theoretical interpretation. This could be used to model the interaction of distant continents.

We considered a delay model in the simulation under consideration. In a subsequent analysis it is examined whether the qualitative behavior of the simulation is retained if the length of stay in the compartments is replaced by transition probabilities. In models of ordinary and partial differential equations, delays generally lead to qualitatively significantly different results.

If Markov models lead to qualitatively similar results in the context used for the epidemiological situation under consideration, eigenvalues and eigenfunctions of the corresponding analytical manifolds could be helpful for analyzing the stability of the parameters used.

With suitable boundary conditions, eigenvalues and eigenfunctions of the Laplace operator are well known for the torus under consideration. The Laplace operator is decisive for diffusion processes that play a decisive role and leads to morphological developments in pattern formation, cf. (Murray, 2002), (Murray, 2003). Mean value operators in the sense of differential geometry have not yet been used in mathematical biology. In differential geometry and the theory of relativity, they are used to characterize spatial structures, cf. (Günther and Prüfer, 1999), (Schuster, 1988), (Schuster, 1997). In the simulation under consideration, we used mean value operators with a uniform distribution in the maximum metric used. The equal distribution can be replaced by other distributions which, in a possibly more realistic way, reduce the risk of infection with increasing distance. Again, this is only partially realistic because life does not take place on a torus and there are different near-far relationships that can be analyzed with graph-theoretic methods, cf. (Solimano and Bretta, 1982), (Rüdiger et al., 2020), (Welch et al., 2011), (Boguna et al., 2003), (Barrat and Vespignani, 2008).

It is also of essential importance in which way the "small world model" is used, in which it is described in which "small" number of steps each individual can be reached by any other individual, here relevant for chains of infection. In the present context, however, a theoretically possible path must be supplemented with a probability with which this path will be implemented in practice.

In a subsequent paper we will analyze the considered epidemiological development on real life graph networks. As a small network we will use anonymized physicians as nodes of the graph, the edges are given by a through a neighborhood relationship in terms of the number of common patients. As a large network we will use anonymized patients related by physicians visited by both patients using a random selection. In graph theory one also can use the Laplace operator and mean value operators.

Current virological results on Covid-19, as stated in (Chinazzi et al., 2020), (Rosenbaum, 2020), (Pan et al., 2020), (Behrens et al., 2020), (Tang et al., 2020), (Xue et al., 2020), (Kucharski et al., 2020) may influence the spatial-temporal modeling on the level of individuals in future and will give new insights in the dynamics of propagation. But the dynamic of the contagion occurs to a certain extent independently of the knowledge of the known details on an individual level. The influence of measurable variables in individual contacts on global expansion and their validation is a challenge for future research.

It could be that the currently predominantly used PCR tests identify the individuals in the  $I_1$  compartment in our interpretation or the individuals that have already passed into the *R* compartment. The dynamics observed could indicate that, due to cross immunity or other immunological mechanisms, that the  $I_2$  compartment, which could be very important for the dynamics of spread, has so far been little identified in practice.

In different countries there were different dramatic initial situations in the early phase of Covid-19. So far, this has been largely discussed as the result of various politically decided preventive measures. But it could also be that different initial conditions existed with regard to the R-compartment as a result of pre-existing immunity. As already stated, an overarching cross-immunity with regard to Covid-19 could also be modeled in the S compartment. This would have theoretical advantages, but would make the search for meaningful parameters for modeling based on the current state of knowledge more difficult.

Differing spreading dynamics, regardless of the measures taken, may also have played a role.

If measures are aimed at greatly reducing the contagion, this subsequently leads to poor immunity at least without effective vaccinations. Since the contact restriction was practically inconsistent, sufficient immunity was nevertheless not prevented with the exception of very restrictive measures in some countries, which may have since led to a high second wave. The amount of people in overcrowded local transport means may be seen in different interpretations. Current observations can be interpreted to the effect that particularly drastic contact restrictions due to immunity not being achieved could lead to a second wave.

The compartment status has a discrete value (S,  $I_1$ ,  $I_2$ ,  $R_1$ ,  $R_2$ ), while eigenfunctions and their discretizations have a real values. If one intends to use the method of separating the variables to carry out a series expansion using the eigenvalues of the Laplace operator, additional considerations are necessary. A similar problem arises in the bisection problem of graphs. A good starting solution is to separate the eigenfunction for the largest non-trivial eigenvalues into points with positive and negative values. In this respect, it could be a sensible approach to use the eigenfunctions for suitable eigenvalues in a hierarchical procedure (since there are more than two discrete states) for the identification of inherently periodic solutions.

### REFERENCES

- Ahmed, E. and Agiza, H. (1998). On modeling epidemics, including latency, incubation and variable susceptibility. *Physica A*, 253:347–352.
- Andersen, R. and May, R. (1979). Population biology of infectious diseases. Part I. *Nature*, 280:361–367.
- Arnautu, V., Barbu, V., and Capasso, V. (1989). Controlling the spread of epidemics. *Appl.Math.Optimiz.*, 20:297– 317.
- Aronson, D. (1985). The role of diffusion in mathematical population biology: Skellam revisited. Lecture Notes in Mathematics 57 (eds. Capasso, V., Grosso, E. and Paveri-Fontana, S.L.).
- Bailey, N. (1975). *The Mathematical Theory of Infectious Diseases*. Griffin, London.
- Barrat, R. and Vespignani, M. (2008). *Dynamical Processes* on Complex Networks. Cambridge University Press.
- Behrens, G., Cossmann, and A. Stankov, M. V. e. (2020).

Perceived versus proven SARS-CoV-2-specific immune responses in health-care professionals. *Infection*, pages 631–634.

- Beretta, E. and Capasso, V. (1986). On the general structure of epidemic systems. global asymptotic stability. *Comp. and Maths. with Apps.*, 12A:677–694.
- Boguna, M., Pastor-Satorras, A., and Vespignani, A. (2003). Epidemic spreading in complex networks with degree correlations, in: Statistical Mechanics of Complex Networks. Lecture Notes in Physics, vol. 625.
- Capasso, V. (1993). *Mathematical Structures of Epidemic Systems*. Lecture Notes in Biomathematics 97.
- Capasso, V. and Maddalena, L. (1983). Periodic solutions for reaction-fiffusion system modelling the spread of a class of endemics. *SIAM J. Appl. Math.*, 43:417–427.
- Chinazzi, M., Davis, J., and Ajelli, M. e. a. (2020). The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. *Science*, 368 (6489):395–400.
- Dieckman, O., Heesterbeek, J., and Metz, J. (1990). On the definition and the computation of the basic reproduction ratio R0 in models for indectious diseases in heterogeneous populations. J.Math.Biol., 28:365–382.
- Field, R. and Burger, M. E. (1985). Oscillations and Traveling Waves in Chemical Systems. John Wiley, New York.
- Günther, P. and Prüfer, F. (1999). Mean Value Operators, Differential Operators and D'Atri Spaces. Annals of Global Analysis and Geometry, 17:113–127.
- Keener, J. and Sneyd, J. (1998). *Mathematica Physiology*. Springer, New York.
- Kermack, W. and McKendrick, A. (1933). Contributions to the mathematical theory of epidemics. *Proc.R.Soc.Lond.A*, pages 94–122.
- Kucharski, A., Russell, T., and Diamond, C. e. (2020). Early dynamics of transmission and control of COVID-19: a mathematical modelling study. *The Lancet infectious diseases*.
- Mikeler, A., Venkatachalam, S., and Abbas, K. (2005). Modelling Infectious Diseases Using Global Staochastic Cellular Automata. *Journal of Biological Systems*, 13:421–439.
- Murray, J. (2002). Mathematical Biology, I: An Introduction. Springer New York Berlin Heidelberg.
- Murray, J. (2003). Mathematical Biology, II:Spacial Models and Biomedical Applications. Springer New York Berlin Heidelberg.
- Pan, A., Liu, L., and Wang, C. e. a. (2020). Association of publichealth interventions with the epidemiology of the COVID-19 outbreak in Wuhan, China. *JAMA*, 323:1–9.
- Redheffer, R. and Walter, W. (1984). Solution of the stability problem for a class of generalized volterra preypredator systems. *J.Diff.Equations*, 52:245–263.
- Rosenbaum, L. (2020). Facing Covid-19 in Italy ethics, logistics, and therapeutics on the epidemic's frontline. *N Engl J Med.*, 382:1873–1875.
- Rüdiger, S., Plietzsch, F., Sokolov, I., and Kurths, J. (2020). Epidemics with mutating infectivity on small-world networks. *Scientific Reports*, 10 (1):1–11.

- Schuster, R. (1988). On differential equations related to mean value operators for differential forms in hyperbolic spaces and applications to problems in spectral geometry. *Prace Naukowe Politechniki Szczecinskiej*, 380:225–251.
- Schuster, R. (1997). About Systems of Differential Equations related to geodesic differential forms. Mean values and harmonic spaces. Part I. *Journal for Analysis* and its Applications, pages 83–106.
- Solimano, F. and Bretta, E. (1982). Graph theoretical criteria for stability and boundedness of predator-prey systems. *Bull Math. Biol.*, 44:579–585.
- Tang, B., Wang, X., and Li, Q. e. a. (2020). Estimation of the transmission risk of the 2019-ncov and its implication for public health interventions. *Journal of clinical medicine*, 9 (2):462.
- Wang, Y., Cao, J., and Alofi, A. e. (2015). Revisiting nodebased sir models in complex networks with degree correlations. *Physica A*, 437:75–88.
- Welch, D., Bansal, S., and Hunter, D. (2011). Statistical inference to advance network models. *Epidemics*, 3 (1):38–45.
- Xue, F., Jing, S., and et.al., M. J. (2020). A data-driven network model for the emerging COVID-19 epidemics in wuhan, toronto and italy. *Mathematical Biosciences*, 326:108391.