Eötvös Loránd University of Sciences

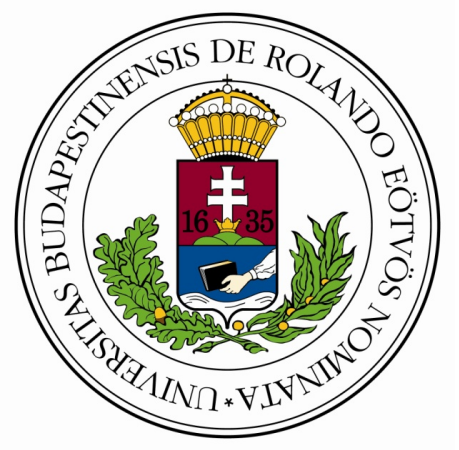
Numerical Models for the Spread of Ebola by using Operator Splitting

Prepared by

László Zénó Farkas

Master Sciences in Applied Mathematics

Supervisor:
István Faragó
Eötvös Loránd University Faculty of Science,
Department of Applied Analysis and
Computational Mathematics



2017
Budapest

Acknowledgements

I would like to thank Dr.Istvan Farago, professor of Eotvos Lorand University, that I could work with him on this topic during my daily work in the research group. I would like to thank the many consultations which signi cantly contributed to the deeper understanding of epidemic spread modelling, as well the support which gave me strength to progression of thesis and work.

Contents

Chapter 1

Introduction

The Ebola virus causes an acute, serious illness, which is often fatal if untreated. Thus, it is important to give an epidemic model that considers not only the spread of the disease, but also feasible delivery system, the speed of manufacturing of the vaccine or drug for Ebola so that we can optimize its eradication.

1.1 Biological background of Ebola

The Ebola disease is a zoonose epidemic which extends basically from animals to people. The Ebola virus genera involves five species at present. The most dangerous for people from them is the so called Zaire Ebola virus (ZEBOV). In this thesis we will discuss about ZEBOV and for the shake of simplicity henceforth we will use simple Ebola instead. The first registered person with Ebola virus was the 44 years old teacher, Mabalo Lokela. The infection was caused perhaps by a reused unsterilized hollow needle [1]. This is a really usual source of infection in underpossessed civilizations. A further potential source of infection could be the non-competent using of medical equipments, nursing service having low quality, void precautions (for example rubber gloves) or traditional burial rituals especially in developing countries of Africa. The most probably putative virus hosts are fruit-eating bats but some plants and arthropods became suspicious, as well. Other research showed that infected bats did not get ill from the Ebola virus thus we could conjecture the immunity of some animals for the virus. The occurrence of the virus in natural environment and possible infections to people are not known yet. However, people are infected definitely not directly by the virus hosting bats instead by infected mammals which more often have direct contact with populations. On the other hand, it is also known that bats are usually consumed by the residents, especially in West-Africa, that is why we can assume in further the virus infection by animals. After getting the disease from animals, the virus will spread inside the civilization, nevertheless, Ebola is not able to keep up permanently inside human populations. It

is important to mention that diseased people can not spread the Ebola virus as they do not show any symptoms and the Ebola virus does not spread among airborne. It follows that it can only circulate among people by direct contact with infected blood or other body- uids (semen, gob) but infection during mouth and conjunctiva is also possible. Furthermore on accordance with the above mentioned facts, the spread of the virus could be promoted by local traditions, such as burial rituals. This is representative mostly in the African continent where this ritual go hand in hand with wash down and kissing of the dead body.

Now we can examine the course of the disease. After infection, 4 10 days latent period is expected. Later the illness begins suddenly with ue-like symptoms which is typical by viral infections. These symptoms are usually discomfort, fever, headache, bellyache, synanche, myalgia and myasthenia. Later symptoms include problems with some organ system, such as the respiratory system, digestive system, nervous system or vascular system. At the acme of the disease, after 5 7 days from the rst symptoms, haemorrhagic fever stigmas emerge and the morality rate in this phase is approximately 70 80%, but in Africa this rate is unfortunately a bit higher.

Survivors might become fully recovered from the disease, however, the healing process can take a long time, even weeks or months and the virus may be present for a good while in the body- uids (for example in semen). However a good counter example was a recovered man who had after 9 and a half months still Ebola virus in his semen [2]. Thereout we can not draw any conclusion about the exact subsistence time of Ebola virus in human organ after healing.

That is however an acknowledged statement of facts that the risk of re-in uence is quietly low but even so during sexual contact is theoretically still possible. After all it is reassuring that in the Sierra Leone area, where the most infected people were registered [3], not one o cial re-infected a air happened. For additional soothing a study was published by an other research documentation in 2014 [4] where it was shown that the organism of a totally cured person produces antibodies against Ebola virus, which protects the individual for at least 3 5 years from re-infection. In addition an other reassuring fact is that there is no vertical transmission from mothers to newborns because of the fast disease progress of Ebola with frequent death rate. Finally it is worth mentioning that Ebola virus is an age specify infection, i.e. the disease progress takes di erent times by di erent age groups [5], but in this work we will not discuss about this factor.

The sickness hasn't presently any permanent treatment. Individuals diagnosed by Ebola virus are immediately isolated from the population (in normal case, according to prescriptions). Without e ective disposals, the prevention of the contagion has a central role in people's life. Diseased and necrolatry by Ebola are miasmatic by contact with body- uids. Therefore direct relations to them should be neglected. The Ebola epidemic in West-Africa in 2014 created a national panic and sped up the propagation of immunization against Ebola virus [3]. The e ect of these was the development of a vaccine which was tested in Guinea where researchers experimented almost 100% successfulness by testing 7651 individuals [6].

1.2 Mathematical background of epidemic spread modelling

This section present a short introduction of epidemic modeling. The whole section based on the book of Vincenzo Capasso [7].

The general idea of the epidemic spread models is separation of the whole population into more sub-population have same properties in some wise. This kind of models are called compartmental models. Generally these groups determine the aim structure of epidemic models which are called usually SI, SIR, $SIRS$, $SEIR$, $SEIRS$ or $SEICRS$ model according as the spread direction of disease. To understand the essence of this model, rstly analyze of simpler models is recommended.

As we have mentioned, in a compartmental model the total population is divided into a number of discrete categories, such as susceptibles (S), infective (I), infected but not yet infective (E), recovered (R), immune/vaccinated (V), carrier (C) etc. without distinguishing di erent degrees of intensity of infection. In contrast, for macroparasitic infections, such as helminthic infections, it is relevant to know the parasite burden borne by an individual host, there can be an important distinction between infection and disease. Consequently, mathematical models for host-macroparasitic associations need to deal with the full distribution of parasites among the host population [8].

A key problem in modelling the evolution dynamics of infectious diseases is the mathematical representation of the mechanism of transmission of the contagion. The concepts of so called force of infection and eld of forces of infection which were introduced in [9], will be the guideline of this subsection. Suppose at rst that the population in each compartment does not exhibit any structure (space location, age, etc.). The infection process is driven by a force of infection (denoted in further by f due to the pathogen material produced by the infective population and available at time t which acts upon each individual in the susceptible class. Thus a typical rate of the infection process is given by the

$$(\text{incidence rate})(t) = f(t)S(t) \tag{1.1}$$

where f include linear or (in complex cases) nonlinear dependence of I, i.e.

$$f(t) = g(I(t)) \tag{1.2}$$

The general model (1.2) for the force of infection may be extend to include a nonlinear dependence upon both I and S. When dealing with populations which exhibit some structure either discrete (e.g. social groups) or continuous (e.g. space location, age), the target of the infection process is the speci c subgroup x in the susceptible class, so that the force of infection has to be evaluated with reference to that speci c subgroup. This induces the introduction of a classical concept in physics. The eld of forces of infection $f(x;t)$ such that the incidence rate at time t

at the speci c location x will be given by

$$(\text{incidence rate})(x;t) = f(x;t)s(x;t) \tag{1.3}$$

It is of interest to identify the possible structures of the eld of forces of infection which depend upon the speci c mechanism of transmission of the disease among di erent groups. When dealing with populations with space structure the relevant quantities are spatial densities, such as $s(x;t)$ and $i(x;t)$, the spatial densities of susceptibles and of infectives respectively, at a point x of the habitat , and at time t 0. The corresponding total populations are given by

$$S(t) = \int s(x;t)dx \quad \text{and} \quad I(t) = \int i(x;t)dx: \tag{1.4}$$

In one population models we shall start considering the evolution of an epidemic in a closed host population of total size N. One of the most elementary compartmental models is the so called SIR model which was rst due to Kermack-McKendrick [10]. The total population is divided into three classes:

S: Susceptibles, i.e. those individuals who are capable of contracting the disease and might becoming themselves infectives later

I: Infectives, i.e. those individuals who are capable of transmitting the disease to susceptibles

R: Removed, i.e. those individuals who have contracted the disease or, if recovered, are permanently immune.

A model based on these three compartments is generally called SIR model. In order to write down a mathematical formulation for the dynamics of the epidemic process we introduce di erential equations for the rates of transfer from one compartment to another:

$$\begin{cases} \dfrac{dS}{dt} = f_1(S;I;R) \\ \dfrac{dI}{dt} = f_2(S;I;R) \\ \dfrac{dR}{dt} = f_3(S;I;R) \end{cases} \tag{1.5}$$

Typically a law of mass action (see in papers [11], [12]) has been assumed for the infection process, i.e. the transfer process from S to I. On other hand the transfer from I to R is considered usually to be a pure exponential decay.

If latency and carriers are allowed, additional classes (E) of latent and (C) of carrier individuals

may be included and the abbreviated model name is $SEICR$. In case of the possibility of reinfection the model is called $SEICRS$. In this thesis the last model is developed and investigated because as far as we know it was never analyzed and expanded before, probably by reason of its drastic complexity. Similarly to the SIR model, we detail the structure of subgroups inside the $SEICRS$ model in Section 2.

1.3 Sequential splitting

Splitting methods are generally used to solve partial differential equations or equation systems, such as in papers [13], [14], [15]. The main idea is to lead the complex problem to the sequence of sub-problems with simpler structure. In the following the general method of sequential splitting (see more detailed in [16]) is presented briefly for the solution of PDEs. The mathematical model can be described in the form of the following abstract Cauchy problem for $t \in [0; T]$ and $x \in [0; L]$

$$\begin{cases} \dfrac{\partial w(x;t)}{\partial t} = \displaystyle\sum_{i=1}^{\infty} A_i w(x;t) \\ w(x;0) = w_0(x); \quad \dfrac{\partial w(0;t)}{\partial x} = g_1(t); \quad \dfrac{\partial w(L;t)}{\partial x} = g_2(t) \end{cases} \tag{1.6}$$

where $w : \mathbb{R} \times \mathbb{R} \to \Omega$ is the Ω-valued unknown function for every fixed $t \in [0; T]$ and Ω denotes the possible states space, which is usually assumed to be a Banach space. Furthermore $w_0(x) \in \Omega$ and $g_1(t), g_2(t) \in \Omega$ define the initial and boundary conditions of the problem and operators $A_i : \Omega \to \Omega$ define the different sub-processes [32].

Operator splitting techniques were developed to find the solution of problem (1.6), when A_i consists of non-linear operator(s). Usually operators are splitted by the different mathematical structures (e.g. linear and non-linear part of the equation are grouped separately) or by the same partial differential operators (grouping different time and space derivatives together), but the splitting is arbitrary. Then the obtained simpler systems are discretized on potentially different meshes.

One of the main advantage of operator splitting techniques is that different numerical schemes and discertizations with different length and time scales can be applied, selecting the most adequate one for a given sub-problem. The main drawback, however may be the loss of convergence and/or accuracy.

For the numerical solution of problem (1.6) the following mesh is defined for the macroscopic (approximation on a normal mesh) and microscopic problem (approximation on a finer mesh), respectively. First, an appropriate grid is generated for macroscopic problem.

Let $!^{mac}_{h;}$ be a mesh, which consists of $(x_i; t_k)$ mesh-points, where h and denote the chosen spatial and time resolution of the mesh, according to the following:

$$x_i = ih; \quad h = \frac{L}{N_L} \quad i = 0;1;2;:::;N_L$$
$$t_k = k \; ; \quad = \frac{T}{N_T} \quad k = 0;1;2;:::;N_T \tag{1.7}$$

where N_L and N_T mark the numbers of division parts in space and time. Then we introduce a ner mesh for the microscopic problem. Let this mesh denoted by $!^{mic}_{h;}$ which consists of the $(x_i; t_n)$ mesh-points, where h and denote the chosen spatial and time resolution, respectively. In this case:

$$x_i = ih; \quad h = \frac{L}{N_L} \quad i = 0;1;2;:::;N_L$$
$$t_n = n \quad ; \quad = \frac{}{N} \quad n = 0;1;2;:::;N_T \quad N \tag{1.8}$$

where N marks the number of subdivision parts in time and space. Let's perceive that $N_T \quad N = N_T \quad = T$ which means that the time interval is the same as by mesh $!^{mac}_{h;}$ only with ner time steps.

There are two things worth mentioning: First, $!^{mic}_{h;}$ contains every point from mesh $!^{mac}_{h;}$ and additionally extra points. Alternatively the two mesh-points are not necessarily needed to overlap, but this case is not investigated here. Second, spatial resolution of the mesh is not changed, because our aim is to use in this work some nite di erent methods (FDMs) which convergence criteria is linked with time through $\frac{}{h^2}$.

Hereinafter the introduction of a corresponding vector space $(!^{mic}_{h;})$ is needed, where the approximated mesh-functions are interpreted on $!^{mic}_{h;}$ (de ned in (1.8)). The goal is to nd series of mesh-functions $(y^n_i)_j := (y_{h;})_j (x_i; t_n) \; 2 \; (!^{mic}_{h;})$ which approximates well the j-th components of vector function $(w)_j (x_i; t_n)$ at the mesh-point $(x_i; t_n) \; 2 \; !^{mic}_{h;}$.

First and last, the original problem (or the operator of the problem) is splitted into macroscopic (Problem 1) and microscopic (Problem 2) sub-problems. The sequential splitting method solves the sub-problem iteratively by applying the steps depicted on Figure 1.1.

The following algorithm describes the solution order sub-problems where $t \; 2 \; [0; T]$, $x \; 2 \; [0; L]$ and $j = 1;2;:::;n$ on the above de ned meshes:

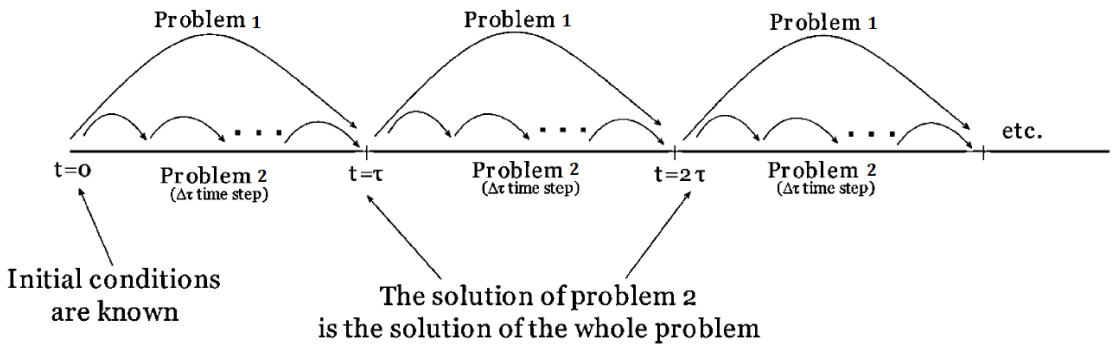


Figure 1.1: Flow chart of sequential splitting algorithm on macroscopic (Problem 1) and microscopic (Problem 2) sub-problems [15].

Problem 1 - Normal mesh (macroscopic)

$$\begin{cases} \dfrac{\partial w_1^{(1)}{}_j}{\partial t}(x;t) = \sum_{i=1}^{k} A_i \; w_1^{(1)}{}_j(x;t) \\ w_1^{(1)}{}_j(x;0) = (w_0)_j(x) \\ \dfrac{\partial w_1^{(1)}{}_j}{\partial x}(0;t) = (g_1)_j(t); \quad \dfrac{\partial w_1^{(1)}{}_j}{\partial x}(L;t) = (g_2)_j(t) \end{cases} \tag{1.9}$$

Problem 2 - Finer mesh (microscopic)

$$\begin{cases} \dfrac{\partial w_2^{(1)}{}_j}{\partial t}(x;t) = \sum_{i=k+1} A_i \; w_2^{(1)}{}_j(x;t) \\ w_2^{(1)}{}_j(x;0) = w_1^{(1)}{}_j(x;\;) \\ \dfrac{\partial w_2^{(1)}{}_j}{\partial x}(0;t) = (g_1)_j(t); \quad \dfrac{\partial w_2^{(1)}{}_j}{\partial x}(L;t) = (g_2)_j(t) \end{cases} \tag{1.10}$$

where the subscripts of w corresponds to the solution of each sub-problem and the superscript is the splitting step. Furthermore Problem 2 is solved independently N times to reach the solution in point , because N = . In the second step of the algorithm we solve the PDE applying the operator in Problem 1 iteratively but now on the [;2] time interval with initial condition $w_2^{(1)}(x;\;)$ and so forth in the following algorithm's steps. By solving the previous n steps iteratively, the constructed $w_2^{(n)}(x;n\;)$ is the solution of sequential splitting on the given ($!_{h;}^{mic}$) mesh.

Chapter 2

Development of the time dependent Ebola epidemic spread model

Based on the SIR model, in this chapter we construct the extended form of it. We introduce latent and carrier subgroups firstly and in the second and third sections we combine the model with other subgroups, such as quarantined and vaccinated individuals. At last we build the vital dynamic into the model, which means a natural birth and mortality rate inside the population.

2.1 The SEICRS model

In mathematical epidemic modeling there exist many compartmental models for disease spreading. From these, in this work the $SEIR$-model is used as default model, e.g. [7], with extra carriers, denoted by C. In favour of combining them, the $SEICR$-model was developed, where initials S, I and R were introduced in Chapter 1 and the rest are defined as follows:

E: Latent individuals, who undergo a latent period, before being themselves capable of transmitting the disease

C: Carriers, i.e. those individuals, who carry and spread the infection disease, but has no clinical symptoms

This model can be extended to the $SEICRS$-model with the assumption of possible reinfection. From now our aim is to extend and combine the basic $SEICRS$ epidemic model with more influential factors, based on paper [30].

When dealing with populations with space structure (this is really important by migration models), the relevant quantities are spatial densities. Firstly we shall define a bounded 2-dimensional

domain in R^2 marked by . Let's use the following notations by di erent groups:

$$G(x;t) = \text{number of individuals in group } G, \text{ at a location } x \ 2 \quad \text{and at time } t \quad 0$$

where G represents one of S, E, I, C or R. Only as an example this means actually the number of susceptibles in a village or in a city inside the country at rst of August. It is remarkable that x is a 2-dimensional vector in space in domain which coordinates actually represent geographical degree of latitude and of longitude, in other words they allocate an abode on the Earth. By using these notations the number of the whole population of the country, denoted by $N_!(t)$ where $!$ marks the o cial registered coordinates of a country, can be speci ed as follows. If we denote the number of individuals inside the di erent groups at an $!$ territory by

$$S_!(t) = \int_! s(z;t)dz; \quad E_!(t) = \int_! e(z;t)dz; \quad I_!(t) = \int_! i(z;t)dz$$
$$C_!(t) = \int_! c(z;t)dz; \quad R_!(t) = \int_! r(z;t)dz \tag{2.1}$$

then

$$N_!(t) = S_!(t) + E_!(t) + I_!(t) + C_!(t) + R_!(t) \tag{2.2}$$

In the further work we assume that habitat $!$ is a bounded and xed parameter and we simplify our notations by omitting it from the superscript.

Corresponding to the classical "law of mass action", which actually means the homogeneous distribution of the epidemic spread between dissimilar groups, many epidemic models have a force infection operator based on linear dependence of individuals from various classes. Ebola virus epidemic is similar to AIDS, which has a non-linear force infection operator during modeling. This means that the infection process from S to E is driven by a given non-linear operator due to the pathogen material produced by the latent individual and susceptibles and available at location x and at time t.

Analogously to the previous detailed, a further operator can be de ned which includes the quality and quantity of individuals transmitting from one class to the other one. The rudimentary model described in the previous section will be transformed to adapted form as developed by Legrand et al, which was previously used to describe the 2000 Uganda Ebola outbreaks [17]. The used model takes into consideration the number of people infected due to direct contact with an infected/carrier individual, the number of people infected due to direct contact with latent individuals etc. Individuals in the latent stage will eventually show the symptoms of the disease and enter into infectious stage. Using notations in (2.1)-(2.2), the time dependent di erential equation of the $SEICR$-model system can be formalized as follows with the appropriate initial conditions:

$$
\begin{cases}
\dfrac{dS}{dt}(t) = \quad \dfrac{_I(t)}{N(t)} I(t) + \dfrac{_C(t)}{N(t)} C(t) \quad S(t) + \quad (t)R(t) \\
\dfrac{dE}{dt}(t) = \quad \dfrac{_I(t)}{N(t)} I(t) + \dfrac{_C(t)}{N(t)} C(t) \quad S(t) \qquad (t)E(t) \\
\dfrac{dI}{dt} = \quad (t)E(t) \quad [''(t) + \quad (t)]\, I(t) \\
\dfrac{dC}{dt}(t) = \, ''(t) I(t) \qquad (t)C(t) \\
\dfrac{dR}{dt}(t) = \quad (t)C(t) \qquad (t)R(t)
\end{cases}
\tag{2.3}
$$

$$
S(0) = S_0; \;\; E(0) = E_0; \;\; I(0) = I_0; \;\; C(0) = C_0; \;\; R(0) = R_0: \tag{2.4}
$$

The ow chart in Figure 2.1 represents well the one directional connection between groups.

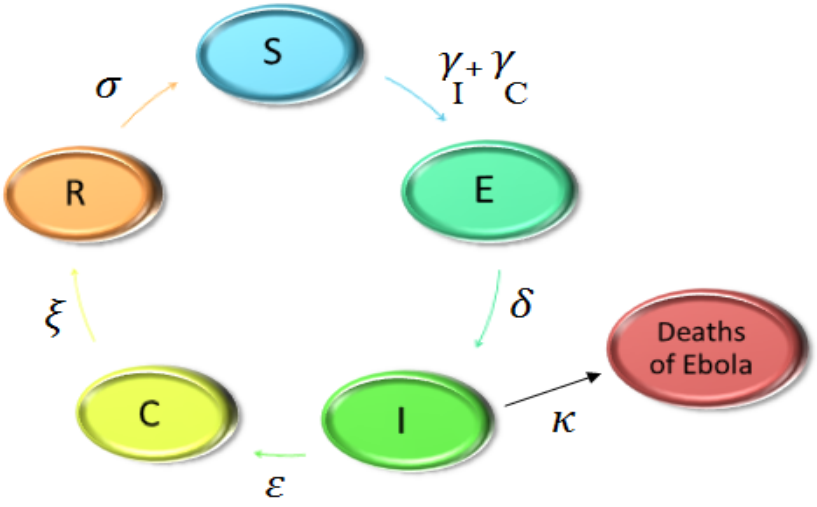


Figure 2.1: Flow chart about the possible transitions between groups

Here, we have $_I(t) = p_I(t) \quad c_I(t)$ and $_C(t) = p_C(t) \quad c_C(t)$ where $p_I(t)$ and $p_C(t)$ denote the probabilities of successfully getting infected when coming into contact with an infected or carrier individual, respectively. Additionally $c_I(x;t)$ and $c_C(x;t)$ are the force infection functions of infected and carrier individuals, respectively. Furthermore (t) denotes the per-capita infectious rate between individuals in latent period and infected humans. In that case, $1= (t)$ becomes the average time for a latent individual to become infectious. $''(t)$ marks the rate of individuals who recovered from the virus and are on the mend, but are still infectious. On the other hand (t) denotes the death rate of the epidemic. Finally (t) stands for the totally recovered humans rate

while (t) implements the proportion of people who are over the protection meaning 10 years against the virus and get into again to the group of susceptibles.

2.2 Quarantine and vaccination

The developed model in (2.3)-(2.4) suggests that Ebola will eventually be out of control, as time goes by. Until now there is no way to cure Ebola, but we do have an e ective way to prevent its spread, which is supposed to be the introduction of individuals in quarantines be denoted by $Q(t)$. This denotes the infectious population being hospitalized by the governments and other medical organizations at time t. Let the rate of infectious individuals being hospitalized denoted by (t) where we assume that the hospitalized individuals share the same death probability with the normal infectious ones but do not infect any exposed individual or susceptible one. Let $_I(t)$ and additionally $_Q(t)$ mark the death rates of infections caused by the Ebola's epidemic in group I and Q, respectively. Furthermore, let $'(t)$ be chosen as the per-capita rate of individuals who are on the mend and become carriers.

In addition, let us denote the seventh class of individuals by $V(t)$, which represents the number of individuals who have been vaccinated before the infection. Therefore individuals belonging this class are not able to get infected and they are not the part of the disease's circulation anymore. Let us denote the vaccination rate by the function (t). With all this in mind we can establish connection between groups after introducing individuals in quarantines and possible vaccination in a ow chart in Figure 2.2.

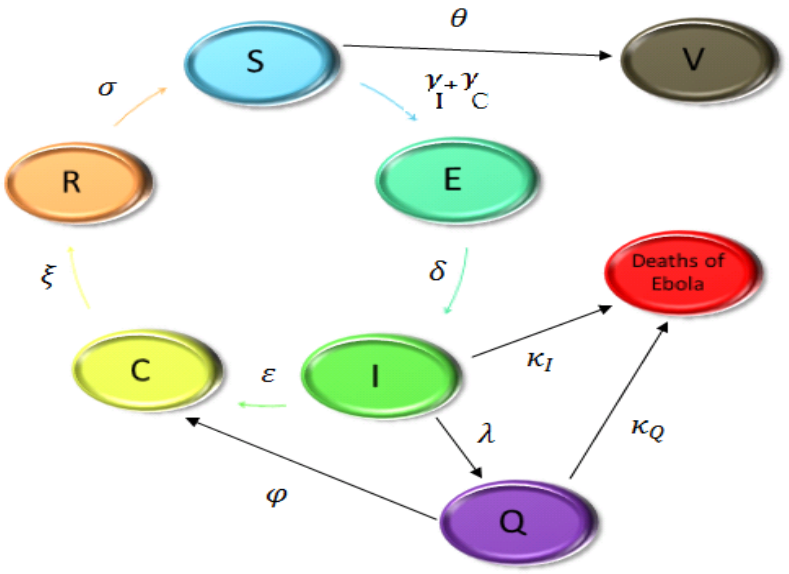


Figure 2.2: Flow chart of the possible transitions between groups expanded by quarantined and vaccinated individuals.

Vaccination program is used to prevent the epidemic and it could alter the courses of the infection, as well. To estimate the best possible approximation of (*t*) for *t*, we shall take into consideration the di erent connections between individuals. These connections are often described in terms of the mixing patterns of the network. We consider two types of mixing patters here, namely, assortative mixing and proportionate mixing. Assortative mixing describes situations in which individuals are more likely to interact with other individuals who are similar to them in some respects, while proportionate mixing (or random mixing) occurs when interactions have no particular preference.

2.3 Vital dynamic

The invariance of the total population can be maintained by introducing the intrinsic vital dynamics of individuals by means of net mortality rate compensated by equal birth input (*t*)*N*(*t*) in the susceptible group, where (*t*) is a known multivalued function. This assumption contains obviously also that there is no vertical transmission of the disease, in other words everybody is assumed to be born clear from infection. We suppose that the natural mortality rate is di erent in each group and let this rate be denoted in every case by (*t*) with the appropriate initial letters of various sub-groups in the subscript. We can assume that (*t*)*N*(*t*) = $\sum_{i=1}^{7}$ $_{G_i}$(*t*)*G*$_i$(*t*) for all *t* 0, where *G*$_i$ denotes the initial identifying the *i*-th group to be modelled, i.e. *G*$_i$ 2 *fS; E; I; C; R; Q; V g* for *i* = 1; 2; 3; 4; 5; 6; 7. Similarly as before as before, we establish the connection between the groups in Figure 2.3 after assuming the vital dynamics.

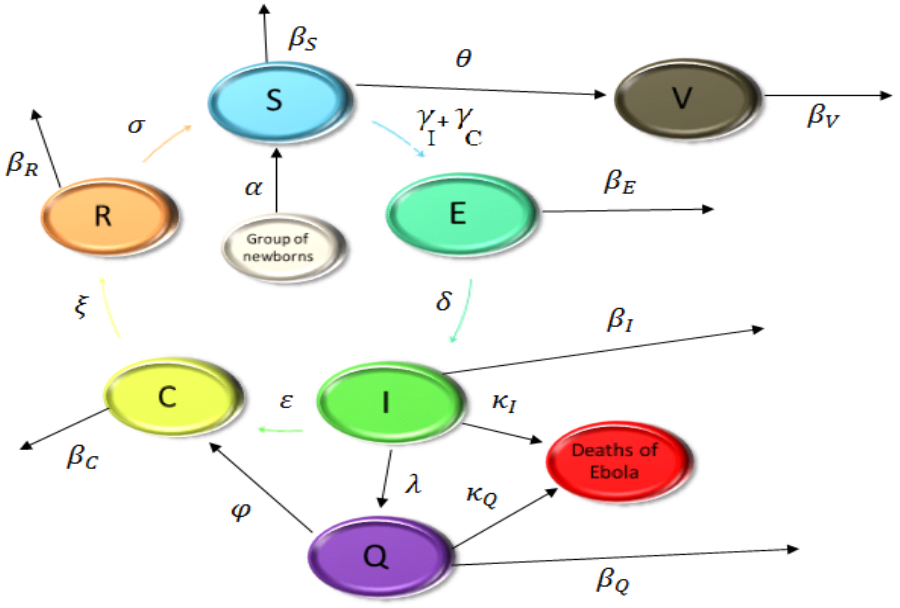


Figure 2.3: Flow chart of the possible transitions between groups expanded by assuming the vital dynamic.

With these three modi cations (i.e. quarantine, vaccination, vital dynamics) we can rewrite the extended form of the system (2.1) with appropriate initial conditions (2.2). Thus we get the following system of ordinary di erential equations for the spread of Ebola:

$$
\begin{cases}
\frac{dS}{dt}(t) = \quad \frac{_I(t)}{N(t)} I(t) + \frac{_C(t)}{N(t)} C(t) + \ (t) + \ _S(t) \ S(t) + \ (t) R(t) + \ (t) N(t) \\
\frac{dE}{dt}(t) = \ \frac{_I(t)}{N(t)} I(t) + \frac{_C(t)}{N(t)} C(t) \ S(t) \quad [\ (t) + \ _E(t)] E(t) \\
\frac{dI}{dt}(t) = \ (t) E(t) \quad [''(t) + \ (t) + \ (t) + \ _I(t)] I(t) \\
\frac{dC}{dt}(t) = \ ''(t) I(t) + \ '(t) Q(t) \quad [\ (t) + \ _C(t)] C(t) \\
\frac{dR}{dt}(t) = \ (t) C(t) \quad [\ (t) + \ _R(t)] R(t) \\
\frac{dQ}{dt}(t) = \ (t) I(t) \quad [\ _Q(t) + \ '(t) + \ _Q(t)] Q(t) \\
\frac{dV}{dt}(t) = \ (t) S(t) \quad \ _V(t) V(t)
\end{cases}
\tag{2.5}
$$

$$
S(0) = S_0; \ E(0) = E_0; \ I(0) = I_0; \ C(0) = C_0; \ R(0) = R_0; \ Q(0) = Q_0; \ V(0) = V_0: \tag{2.6}
$$

At this point we remark, that this system depends only on time, however take into consideration migration, mobility, moving activity etc. the epidemic spread models suppose to be space dependent, as well. In Chapter 3 our aim is to extend model (2.5)-(2.6) by population migration.

Chapter 3

Integration the space dependency into the model

3.1 Population migration effect

In this section we make a systematic study to some population migration models. The whole section based on the work [18]. These models have the form of di erential integral equations. They describe the evolution of the density of a system of population living in a spatial domain R^n. Individuals in this population system can move from one location to the other with a rate uniquely determined by their departure and arrival locations. We use the terminology migration to address spatial movement of the population and call the rate mentioned above migration rate. The migration rate function determines to a great extent the dynamical behaviour of the population system. We shall mainly consider a special class of population system in which individuals can migrate from any one location to any other location through nite steps of intermediate migrations. We call such a population system as ergodic system.

Let be a domain in R^n, in which the population lives. We introduce a migration rate function $v(x;y)$ in , or more precisely the migration rate from location y 2 to location x 2 , de ned as follows.

De nition 3.1 *For an o -diagonal point $(x;y)$ 2 , $x \neq y$, let O_x and O_y be two disjoint sub-domains of containing x and y, respectively. Assume that within an unite time interval the total amount of population migrated from O_y to O_x is $M(O_x;O_y)$ and the total amount of population in O_y before migration is $M(O_y)$. Then*

$$v(x;y) = \lim_{\substack{diam(O_x)! \ 0 \\ diam(O_y)! \ 0}} \frac{M(O_x;O_y)}{jO_xjM(O_y)} \tag{3.1}$$

where $jO_x j$ denotes then-dimensional Lebesgue-measure of the domain O_x. For a diagonal point of we de ne the value of $v(x;y)$ to be its o -diagonal limit. Let

$$v_i(x) = \int v(x;y)dy; \quad v_e(x) = \int v(x;y)dx; \tag{3.2}$$

they are called the immigration rate and emigration rate at the location x and y, respectively. Notice that these de nition immediately yield the following relation:

$$\int v_i(x)dx = \int v_e(y)dy: \tag{3.3}$$

From the de nition of the migration rate function we see that for a point $x \in$, if v(x,y)=0 for all $y \in$, then there is no migration from other location to the location x. Consequently in this case $v_i(x) = 0$. For a point $x \in$, if $v(y;x) = 0$ for all $y \in$, then there is no migration from the location x to other location, and in this case $v_e(x) = 0$. If at a location x there holds $v_i(x) > v_e(x)$ then in a small neighborhood of x the amount of population immigrated in is larger than the amount of population emigrated out, whereas if $v_e(x) > v_i(x)$ then in a small neighborhood of x the amount of population emigrated out is larger than the amount of population immigrated in. In the case $v_e(x) = v_i(x)$ we say that immigration and emigration at the location x is balanced. In particular, if the relation $v_e(x) = v_i(x)$ holds for all $x \in$, we call such a migration as balanced migration. A particular case of the balanced migration is symmetric migration, which means that $v(x;y) = v(y;x)$ for all $x;y \in$. Finally we mention that from relation (3.3) we see that if there is a subdomain $_1$ in which $v_e(x) > v_i(x)$ then there must be another subdomain $_2$ in which $v_e(x) < v_i(x)$, and vice versa.

In this thesis we do not pursue a complete understanding to an arbitrary population system with migration. Instead we mainly consider dynamical behaviour of a special class of such system as de ned below.

De nition 3.2 *We say that a population system is ergodic if its migration rate function v satis es the following property: For any point $(x_0;y_0) \in$, $x_0 \neq y_0$, there exist nite number of points $(x_1;y_1)$, $(x_2;y_2):::$, $(x_m;y_m) \in$ such that*

$$y_1 = y_0; y_2 = x_1; y_3 = x_2; :::; y_m = x_{m-1}; x_m = x_0$$

and for each $1 \leq j \leq m$, $v(x;y) > 0$ for all $(x;y)$ in a neighborhood of $(x_j;y_j)$. In this case we also say that the function v is ergodic

From the above defnition we see that if a population system is ergodic then it is possible for an individual in this system at any location to migrate to any other location through nite steps

of intermediate migrations. Clearly, for such a population system we have

$$v_i(x) > 0 \text{ and } v_e(x) > 0 \text{ for all } x \in \quad :$$

It is also clear that if $v(x;y) > 0$ for all $(x;y) \in$ then the population system is an ergodic system. In this case we say that the population system is completely ergodic. One can see some example for non completely ergodic case in [29].

Let us discuss now about the proliferation-stationary population migration models. We denote by $N(x;t)$ the population density at the location $x \in$ at time t. We assume that the population at every location in is in the proliferation-stationary state, i.e., the birth rate and the death rate are equal at every point $x \in$, and only consider the e ect of migration of population. For an arbitrary sub-domain O and an arbitrary time interval $[t_1;t_2]$, we have

$$\underbrace{\int_O N(x;t_2)\,dx - \int_O N(x;t_1)\,dx}_{\text{increment of population}} = \underbrace{\int_{t_1}^{t_2}\int_{O}\int_{nO} v(x;y)N(y;t)\,dydxdt}_{\text{population immigrated in}} - \underbrace{\int_{t_1}^{t_2}\int_{nO}\int_{O} v(x;y)N(y;t)\,dydxdt}_{\text{population emigrated out}}$$

Dividing both sides with $(t_2 - t_1)|O|$ and next letting $\text{diam}(O) \to$ and $t_2 - t_1 \to 0$, we obtain the following di erential-integral equation:

$$\frac{\partial N(x;t)}{\partial t} = \int v(x;y)N(y;t)\,dy - v_e(x)N(x;t), \quad x \in \ ; \ t > 0. \tag{3.4}$$

We call it the proliferation-stationary population migration equation, or simply population migration equation later on. We impose the following initial value condition:

$$N(x;0) = N_0(x), \quad x \in \tag{3.5}$$

where N_0 is given non-negative function. For simplicity we only consider the case where is a bounded domain.

3.2 Properties and extensions

In this section we develop the complex form of epidemic spread model for the spread of Ebola combined with population migration e ect. For the shake of it, rstly we detail some easy and basic assertions, as follows:

(1) Since the equation (3.4) is a linear di erential-integral equation, by using either the standard Picard iteration method or the uniformly continuous semigroup theory, we can easily prove that under suitable assumptions on the migration function v, the initial value problem (3.4)-(3.5) is

globally wee-posed in the function spaces $C(\ )$ and $L^p(\ )$ for $1 \quad p < 1$. More precisely, if $v \ 2 \ C(\quad)$ then for any $N_0 \ 2 \ C(\ )$ the problem (3.4)-(3.5) has an unique solution $N \ 2 \ C(\quad [0; \ 1))$ and the map $N_0 \ 7! \ N$ from $C(\ )$ to $C(\quad [0; T])$ is linear and continuous for any T (similarly, if $v \ 2 \ L^1 \ (\quad)$).

(2) If $N_0(x) \quad 0$ for all $x \ 2 \quad$, then $N(x; t) \quad 0$ for all $x \ 2 \quad$ and $t \quad 0$.

(3) Total amount of the population is constant, i.e., letting $M(t) = \int_{\mathbb{R}} N(x; t)dx$ be the total amount of the population at time t and $M_0 = \int_{\mathbb{R}} N_0(x)dx$ be the initial total amount of the population, we have

$$M(t) = M_0 \text{ for all } t \quad 0: \tag{3.6}$$

Indeed, since $\int_{\mathbb{R}} v(x; y)dx = v_e(y)$, by integration both sides of the equation (3.5) with respect to the variable x, we get

$$\frac{@M(t)}{@t} = \int_{\quad} v_e(y)N(y; t)dy \quad \int_{\quad} v_e(x)N(x; t)dx = 0; \quad t > 0;$$

so that $M(t) = M_0$ for all $t \quad 0$.

(4) If $v_e(x_0) = v_i(x_0) = 0$ for some $x_0 \ 2 \quad$, then $N(x_0; t) = N_0(x_0)$ for all $t \quad 0$. Indeed, since $v(x; y) \quad 0$ for all $x; y \ 2 \quad$, the condition $v_i(x_0) = \int_{\mathbb{R}} v(x_0; y)dy = 0$ implies that $v(x_0; y) = 0$ for all $y \ 2 \quad$. Hence, from the condition $v_e(x_0) = v_i(x_0) = 0$ we see that at the point x_0 the equation (3.5) takes the form

$$\frac{@N(x_0; t)}{@t} = 0 \text{ for } t > 0;$$

so that $N(x_0; t) = N_0(x_0)$ for all $t \quad 0$. This means that if at a location the population does neither migrate in or migrate out, then the population density keeps constant at that location.

If $v_i(x_0) = 0$ and $v_e(x_0) > 0$ for some $x_0 \ 2 \quad$, then $lim_{t!1} \quad N_0(x_0; t) = 0$. Indeed, at the point x_0 the equation (3.5) takes the form

$$\frac{@N(x_0; t)}{@t} = \quad v_e(x_0)N(x_0; t) \text{ for } t > 0;$$

so that $N(x_0; t) = N_0(x_0)e^{\ tv_e(x_0)}$ for all $t \quad 0$, which implies that $lim_{t!1} \quad N_0(x_0; t) = 0$. This means that if the population does not migrate into a location but keeps migrating out of that location, then the population at that location will nally vanish.

(6) If $v_e(x_0) = 0$ and $v_i(x_0) > 0$ for some $x_0 \ 2 \quad$, then $N(x_0; t)$ is strictly monotone increasing in t. Indeed, at the point x_0 the equation (3.5) takes the form

$$\frac{@N(x_0; t)}{@t} = \int_{\quad} v(x_0; y)N(y; t)dy > 0 \text{ for } t > 0;$$

so that $N(x_0;t)$ is strictly monotone increasing. This means that if the population does not migrate out of a location but keeps constantly migrating to that location, then the population at that location keeps increasing.

We mention at this point that we can extend the result of the above detailed proliferation stationary population migration model to the proliferation non-stationary case. Let $r = r(x)$, $x \in$, be the proliferation rate function, i.e., for every $x \in$, $r(x)$ is the proliferation rate (=birth rate minus death rate) of the population at location x. Assume that this function is not identically vanishing in . Then the equation (3.5) should be replaced by the following equation:

$$\frac{\partial N(x;t)}{\partial t} = \int v(x;y)N(y;t)dy \quad v_e(x)N(x;t) + r(x)N(x;t); \quad x \in \quad ; \quad t > 0: \tag{3.7}$$

Furthermore a short discussion to non-ergodic case. If we remove the ergodicity assumption then the situation is very much complex. In this paper we only consider two special cases. Moreover, we assume that the population system is in the proliferation-stationary case.

(1) First we consider the case that the habitat domain is divided into several disjoint parts and population in each part forms an independent population system. Hence we assume that

$$= \bigcup_{j=1}^{m} {}_j; \text{ where } {}_j \setminus {}_k = ; \text{ for } j \neq k;$$

and $v(x;y) = 0$ if $(x;y) \in {}_j \times {}_k$, $j \neq k$, where $j;k = 1;2;:::;m$. Moreover, for every $1 \quad j \quad m$ we assume that $v|_{{}_j \times {}_j}$ is continuous and ergodic in ${}_j \times {}_j$. Thus, the whole population system is divided into several subsystem, with each subsystem being ergodic and different subsystems being mutually independent or having no interchange of population between different subsystems.

(2) Next we consider the case that the habitat domain is divided into two disjoint parts ${}_1$ and ${}_2$, i.e., ${}_1 \setminus {}_2 = ;$ and $= {}_1 \cup {}_2$, such that $v(x;y) > 0$ for $(x;y) \in {}_1 \times {}_1$, ${}_1 \times {}_1$ and ${}_2 \times {}_2$, whereas $v(x;y) = 0$ for $(x;y) \in {}_2 \times {}_1$. We omit the details, one can see some of them in these case in [18].

Finally in this section we consider a complex mathematical model describing spread of epidemics in migration population system assuming the proliferation non-stationary case with ergodic migration. Using notations (2.5), we can transform our extended Ebola epidemic system (2.5) into the form of partial-integro differential equations (PIDE), and we can combine it with the proliferation-stationary model in (3.7) with initial conditions

$$S(0) = S_0; \quad E(0) = E_0; \quad I(0) = I_0; \quad C(0) = C_0; \quad R(0) = R_0; \quad Q(0) = Q_0; \quad V(0) = V_0 \tag{3.8}$$

as follows:

$$
\begin{cases}
\dfrac{\partial S}{\partial t}(x;t) = & \dfrac{\beta_I(x;t)}{N(x;t)} I(x;t) + \dfrac{\beta_C(x;t)}{N(x;t)} C(x;t) + \gamma(x;t) + \mu_S(x;t)\ S(x;t) + \\
& + \alpha(x;t) R(x;t) + \mu(x;t) N(x;t) + \int v(x;y) S(y;t)\,dy - v_e(x) S(x;t) \\
\dfrac{\partial E}{\partial t}(x;t) = & \dfrac{\beta_I(x;t)}{N(x;t)} I(x;t) + \dfrac{\beta_C(x;t)}{N(x;t)} C(x;t) - S(x;t) - [\ \alpha(x;t) + \mu_E(x;t)] E(x;t) + \\
& + \int v(x;y) E(y;t)\,dy - v_e(x) E(x;t) \\
\dfrac{\partial I}{\partial t}(x;t) = & \alpha(x;t) E(x;t) - [\varepsilon(x;t) + \mu_I(x;t) + \gamma(x;t) + \mu_I(x;t)] I(x;t) + \\
& + \int v(x;y) I(y;t)\,dy - v_e(x) I(x;t) \\
\dfrac{\partial C}{\partial t}(x;t) = & \varepsilon(x;t) I(x;t) + \theta'(x;t) Q(x;t) - [\ \gamma(x;t) + \mu_C(x;t)] C(x;t) + \\
& + \int v(x;y) C(y;t)\,dy - v_e(x) C(x;t) \\
\dfrac{\partial R}{\partial t}(x;t) = & \gamma(x;t) C(x;t) - [\ \alpha(x;t) + \mu_R(x;t)] R(x;t) + \\
& + \int v(x;y) R(y;t)\,dy - v_e(x) R(x;t) \\
\dfrac{\partial Q}{\partial t}(x;t) = & \theta(x;t) I(x;t) - [\ \mu_Q(x;t) + \theta'(x;t) + \mu_Q(x;t)] Q(x;t) + \\
& + \int v(x;y) Q(y;t)\,dy - v_e(x) Q(x;t) \\
\dfrac{\partial V}{\partial t}(x;t) = & \gamma(x;t) S(x;t) - \mu_V(x;t) V(x;t) + \int v(x;y) V(y;t)\,dy - v_e(x) V(x;t).
\end{cases}
\tag{3.9}
$$

Since our aim is to approximate the solution of the system, we need to have the well poseness of it. For it we need to estimate the boundary conditions by every sub-group.

3.3 Estimation of boundary conditions

Our aim is to apply the sequential splitting algorithm to approximate the solution of the system of PIDE's (3.8)-(3.9). For this purpose rst we determine the appropriate boundary conditions for points $x \in @$, where $@$ denotes the boundary of habitat . To do that we use the classical Neumann-boundary conditions which de nes the ux (combination of immigration and emigration rate) of individuals at $@$. We suppose that this ux depends on time and on the location uniformly. In mathematical formulation this means the following

$$\frac{@G_i}{@x}(x;t) = \quad _{G_i}(x;t); \quad x \in @ \quad ; \quad t \in [0;T]: \tag{3.10}$$

where $_{G_i}$ supposed to be in space $L^2($ $[0;T])$.

Thus we need to do determine functions $_{G_i}(x;t)$ for every sub-group, namely, for all $G_i \in fS;E;I;C;R;Q;Vg$. We may assume that the emigration rates of susceptibles and latent individuals increases after the outbreak of Ebola and going to be decreased after dangerous state. Vaccinated individuals have no reason to move, that is why their ux at the boundary is much lower. The ux by quarantines is even more restricted because people are not able to move of their own own free will or they are in safety in quarantines. Infected, carriers and removed individuals neither have too much reason to migrate, they are already infected or belong to the small group who survived the virus Ebola. Figure 3.1 represents the density of migration by susceptibles, at xed x point of boundary $@$.

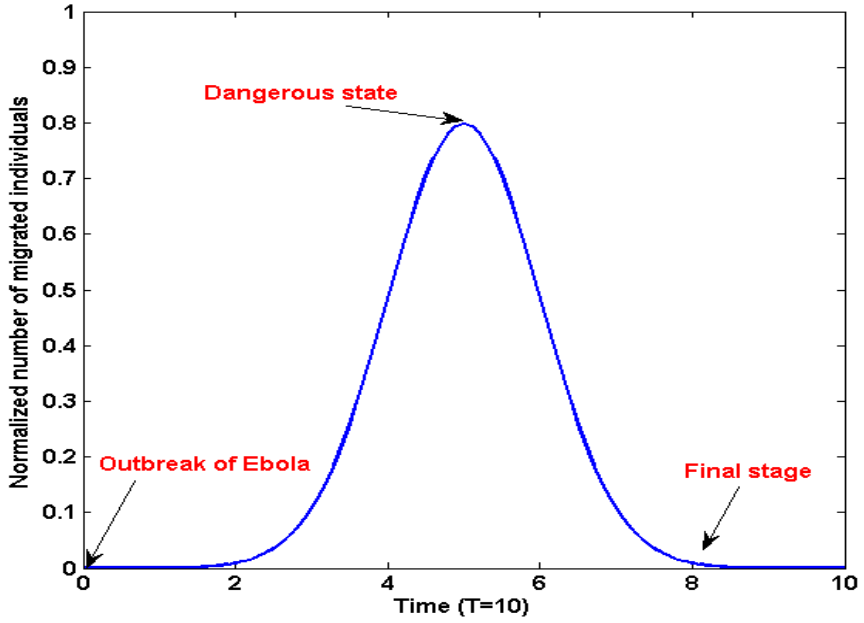


Figure 3.1: Normalized density of migration by susceptible individuals in case $T = 10$

If we accept these assumptions, we can de ne functions $_{G_i}(x;t)$ for all G_i as the modulator of normal distribution where the expected value m_i determines the expected hollow point of the epidemic for all $i = 1;2;3;4;5;6;7$ and the variance is taken as constant, i.e.,

$$_{G_i}(x;t) := \frac{k_i(x)}{p\overline{2}} e^{\frac{(t \quad m_i)^2}{2}}; \quad x \; 2 \; @ \quad ; \quad t \; 2 \; [0;T] \tag{3.11}$$

where $k_i(x)$ denotes the ux constant for all locations at the boundary of the domain for the di erent sub-groups $(S;E;I;C;R;Q;V)$.

Before we would discuss about the numerical solution of the system (3.9) with initial (3.8) and boundary (3.11) conditions, we are going to develop the generalized form of epidemic spread systems, in order to show an e ective way to approximate them. Then we can apply later in this work the chosen numerical schemes on system developed in this chapter.

Chapter 4

Construction of general discretized system

4.1 Formalization and assumptions

Hence the epidemic model for the spread of Ebola has some characteristic property, such as nonlinear dependency of subgroups and population migration e ect, our goal is to develop a generalized model with the same features in extended form. To do that we need to introduce some notations and provisions.

Let us denote the variables by $_i(x;t)$ for $i = 1;2;:::;n$ which are supposed to be the classical solution of the PIDE, hence they are taken from the space $L^1 \quad \setminus C^1(I) \setminus C^1(@\ )$ where $x\ 2$ and $t\ 2\ I$. Thence we will denote this function space by $M(\ ;I)$. Furthermore we de ne two function valued vectors as follows,

$$\sim := [\ _1;\ _2;:::;\ _n]^T;\ \sim\ _i := [\ _1;\ _2;:::;\ _i\ _1;\ _{i+1};:::;\ _n]^T; \tag{4.1}$$

After this we need to introduce some operators and source term functions to represent the various unexpected factors of the model which in uence the size of population or behaviour of individuals. Let us de ne $F_i : M(\ ;I) \ ! \ M(\ ;I)$ as the operator of self-dependency, $G_i : M^n(\ ;I) \ ! \ M(\ ;I)$ as the operator of else-dependency, and as $H_i : M^n(\ ;I) \ ! \ M(\ ;I)$ the operator of nonlinear dependency which operate di erently for all i and

$$M^n := \underbrace{M \quad M}_{\text{n times}}:$$

Finally we denote the source terms by $f_i(x;t)$, the function of initial conditions by $_{i;0}(x)$ and of the boundary conditions by $K_i(x;t)$ for all i.

With all this in mind we can develop our generalized PIDE system, as follows

$$\begin{cases} \dfrac{@\ _i}{@t}(x;t) = (F_i(\ _i))(x;t) + (G_i(\ \sim_i))(x;t) + \hbar H_i(\sim);\sim i(x;t) + f_i(x;t) \\ \\ \ _i(x;0) = \ _{i;0}(x);\ \ x\ 2 \\ \\ \dfrac{@\ _i}{@x}(x;t) = K_i(t)\ \ x\ 2\ @\ \ ;\ \ t\ 2\ I \end{cases} \tag{4.2}$$

where $x\ 2$ and $t\ 2\ I$ for $i = 1;2;:::;n$. One can see that system (4.2) is very complicated to analyze in this form, thus we simplify it in order to the easier analysis of numerical approximation and their properties.

For the shake of it, we suppose that the number of the variables is two ($n = 2$), the habitat $:= [L1;L2]$, i.e. it is one dimensional and $I = [0;T]$. In purpose of the better visibility we do not use by the variables its space and time dependency. Now, using these simpli cations, we examine the following system

$$\begin{cases} \dfrac{@\ _1}{@t} = A_1\ _1 + B_1\ _2 + C_1 \displaystyle\int_{L1}^{L2} \ _1 dx + D_1\ _1\ _2 + f_1(x;t) \\ \\ \dfrac{@\ _2}{@t} = A_2\ _2 + B_2\ _1 + C_2 \displaystyle\int_{L1}^{L2} \ _2 dx + D_2\ _1\ _2 + f_2(x;t) \\ \\ \ _1(x;0) = \ _{1;0}(x);\quad \ _2(x;0) = \ _{2;0}(x);\ \ x\ 2\ [L1;L2] \\ \\ \dfrac{@\ _1}{@x} = K_1(t);\ \ \dfrac{@\ _2}{@x} = K_2(t);\ \ x = L1 \text{ or } L2;\ \ t\ 2\ [0;T] \end{cases} \tag{4.3}$$

where one can easily seen (for $i = 1;2$) that

$$F_i(\ _i) = A_i\ _i + C_i \int_{L1}^{L2} \ _i dx;\ \ G_1(\ _2) = B_1\ _2;\ \ G_2(\ _1) = B_2\ _1;\ \ \hbar H_i(\sim);\sim i = D_i\ _1\ _2:$$

where the coe cients A_i, B_i, C_i, D_i are de ned constants.

In the next section we describe the numerical approximation scheme on system (4.3), namely the one step -method.

4.2 Discretization by using -method

As we know from basic numerical calculus, the general form of the -method applied on ordinary di erential equations (ODEs) is the following:

$$y_n = y_{n\ 1} + {}_n[(1 \quad)f_{n\ 1} + \quad f_n]$$

where y_n is the approximation of the solution at point t_n de ned on the mesh $!_{\ n} = ft_0 = 0; t_n = t_{n\ 1} + {}_n; n = 1; 2; : : : ; N + 1g$, furthermore $f_n := f(t_n; y_n)$. This method can be applied similarly to PDE systems. In that case we need to x the discretization of each variables, i.e., if $y_{n;i} = y(t_n; x_i)$ then

$$y_{n;i} = y_{n\ 1;i} + {}_n[(1 \quad)f_{n\ 1;i} + \quad f_{n;i}]$$

where -method has been applied on time variable on mesh $!_{\ n;h_i} = f(t_n; x_i); t_0 = 0; t_n = t_{n\ 1} + {}_n; x_i = x_{i\ 1} + h_i; n = 1; 2; : : : ; N_t + 1; i = 1; 2; : : : ; N_x + 1g$.

The scheme of discretization by PIDE systems is similar, but the approximation of the integral part has to be chosen from quadrature-formulas. In this thesis we use the simple trapezoidal rule, thus the method is

$$\int_{x_{i\ 1}}^{x_i} y_{n;i} \quad \frac{h_i}{2}(y_{n;i} + y_{n;i\ 1}):$$

In the following we assume that the mesh $!_{\ n;h_i}$ is equidistant, namely ${}_n$ and h_i h for all n and i. With all this in mind we can describe the -method discretization applied on system (4.3), as follows:

$$\begin{cases}
\dfrac{{}^{n;i}_1 \quad {}^{n\ 1;i}_1}{} = (1 \quad)\left[A_1\,{}^{n\ 1;i}_1 + B_1\,{}^{n\ 1;i}_2 + D_1\,{}^{n\ 1;i}_1\,{}^{n\ 1;i}_2 + f_1^{n\ 1;i}\right] + \\
\quad + \left[A_1\,{}^{n;i}_1 + B_1\,{}^{n;i}_2 + D_1\,{}^{n;i}_1\,{}^{n;i}_2 + f_1^{n;i}\right] + \\
\quad + (1 \quad)C_1\dfrac{h}{2}\left({}^{n\ 1;i}_1 + {}^{n\ 1;i\ 1}_1\right) + C_1\dfrac{h}{2}\left({}^{n;i}_1 + {}^{n;i\ 1}_1\right) \\
\dfrac{{}^{n;i}_2 \quad {}^{n\ 1;i}_2}{} = (1 \quad)\left[A_2\,{}^{n\ 1;i}_2 + B_2\,{}^{n\ 1;i}_1 + D_2\,{}^{n\ 1;i}_1\,{}^{n\ 1;i}_2 + f_2^{n\ 1;i}\right] + \\
\quad + \left[A_2\,{}^{n;i}_2 + B_2\,{}^{n;i}_1 + D_2\,{}^{n;i}_1\,{}^{n;i}_2 + f_2^{n;i}\right] + \\
\quad + (1 \quad)C_2\dfrac{h}{2}\left({}^{n\ 1;i}_2 + {}^{n\ 1;i\ 1}_2\right) + C_2\dfrac{h}{2}\left({}^{n;i}_2 + {}^{n;i\ 1}_2\right)
\end{cases} \tag{4.4}$$

with the following initial and boundary conditions:

$$\begin{cases} {}^{0;i}_{1} = {}^{i}_{1;0}; \quad {}^{0;i}_{2} = {}^{i}_{2;0}; \quad i = 0;1;:::;N_x + 1 \\ \dfrac{{}^{n;1}_{1} - {}^{n;0}_{1}}{h} = K_1^{n;0}; \quad \dfrac{{}^{n;N_x+1}_{1} - {}^{n;N_x}_{1}}{h} = K_1^{n;N_x+1}; \quad n = 1;2;:::N_t + 1 \\ \dfrac{{}^{n;1}_{2} - {}^{n;0}_{2}}{h} = K_2^{n;0}; \quad \dfrac{{}^{n;N_x+1}_{2} - {}^{n;N_x}_{2}}{h} = K_2^{n;N_x+1}; \quad n = 1;2;:::N_t + 1 \end{cases} \tag{4.5}$$

where 2 $[0;1]$, A_i, B_i, C_i and D_i are de ned constants for $i = 1;2$ and $t_0 = 0$, $t_{N_t+1} = T$, $x_0 = L_1$ and $x_{N_x+1} = L_2$.

After this we say something about the qualitative properties of the system and we give an elementary estimation to the theoretical error of the numerical scheme. Let express variables ${}^{n;i}_{1}$ and ${}^{n;i}_{2}$ by using rearrangement of the system (4.4). In this case we supposed to assume that expression $A_1 + C_1\frac{h}{2} + D_1\,{}^{n;i}_{2}$ and $A_2 + C_2\frac{h}{2} + D_2\,{}^{n;i}_{1}$ are not equal to zero for all i and n. This rearrangement yields a non-linear algebraic equation system for variables ${}^{n;i}_{1}$ and ${}^{n;i}_{2}$. At this point we remark that showing the non-negativity of the system is a very complex procedure, that is why we just mention here the basic steps of the procedure based on induction. Assuming that if ${}^{0;i}_{j} > 0$ then ${}^{1;i}_{j} > 0$ follows for all $j = 1;2$. We would like to show that assumptions ${}^{n\ 1;i}_{j} > 0$ and ${}^{n;i\ 1}_{j} > 0$ imply the inequality ${}^{n;i}_{j} > 0$ for all j, i, and n. The proof of it could be a further research topic.

To show the theoretically expected error, we turn back to the system (4.4). For it we need to take into consideration the source of possible upcoming error sources. in our case these are:

Error of the continuous model setting,

Error time discretization scheme,

Approximation error of the quadrature formula.

From these three are only the last two considerable, because the rst one can not be estimated mathematically, either numerically. Based on the general numerical calculus, we know that -method is convergent in second order, if $= \frac{1}{2}$, and it is convergent in rst order in case $\neq \frac{1}{2}$. Similarly, the trapezoidal quadrature formula yields $O(h^3)$ order error term.

As a conclusion we can say, that the -method combined with the trapezoidal rule applied on system (4.3) is expected to be $^2 + h^2$-th order in case $= \frac{1}{2}$ and $+ h^2$ in case $\neq \frac{1}{2}$. one can see, that $= \frac{1}{2}$ guarantees the higher order of the numerical convergence, however causes much more calculation and complexity by applying the approximation algorithm. The question is, how could we reach $^2 + h^2$-th order convergence next to a lower running time. In the next chapter we will develop the alternant- -method, which provide us the higher order convergence with more less calculation (running time).

Chapter 5

Alternant-theta method

5.1 Motivation and basics

In this section we are going to give a short introduction into the alternant- method applied on classic ODE. We mention that the whole chapter based on the work [31].

Many scienti c problems can be described by the initial value problem for rst order ODEs of the form

$$\frac{du}{dt}(t) = f(t;u(t)); \quad t \in (0;T) \tag{5.1}$$

$$u(0) = u_0: \tag{5.2}$$

The solution of such problems plays considerable role in the mathematical modelling. As it is known under the global Lipschitz condition, i.e.,

$$|f(t;s_1) \quad f(t;s_2)| \quad L|s_1 \quad s_2| \text{ where } (t;s_1);(t;s_2) \in \mathrm{dom}(f) \tag{5.3}$$

with the Lipschitz constant $L > 0$, the problem (5.1)-(5.2) has unique solution on the domain $\mathrm{dom}(f)$.

However, we cannot de ne the solutions for the majority of di erential equations in analytic form, hence suitable numerical algorithms are needed for accurately approximations. The numerical integration of the problem (5.1)-(5.2) under the condition (5.3) is one of the most typical tasks in the numerical modelling of real-life problems.

One of our aim in this chapter is to de ne some numerical solution at xed points $t^? \in (0;T)$ to the classical Cauchy problem (5.1)-(5.2). Let us consider the sequence of non-equidistant meshes

with alternant mesh-sizes h_n of the form

$$!_{h_n} = ft_0 = 0; t_n = t_{n\ 1} + h_n;\ \ n = 1;2;:::;Ng$$

and our goal is to de ne at the mesh-point $t^? = t_N$ a suitable approximation denoted by y_N on each xed mesh. At this point we remark that a condition should be made for time steps h_n, namely we suppose that there exists a real positive number C such that the inequality

$$h_n \quad C\ \ h;\ \text{for all } n = 1;2;:::;N \quad 1 \text{ and for all } N = 2;3;::: \tag{5.4}$$

holds, where $h := max_n fh_n g$. Condition (5.4) means that we demand an uniformly stepwise re nement for every time partition of the interval $(0;T)$.

The most popular and simplest methods for de ning the mesh-function $y_h : !_h \ ! \ R$ are the so-called one-step schemes, particularly, the theta-method which is notated frequently as -method. To proof its convergence there are many works, such as [21]. To de ne the more general alternant form of theta-method, we change the parameter at each step. These varying values are denoted by $_n$. Hence, the alternant- -method (in the following called ATM) can be de ned as follows.

De nition 5.1 *Let us consider the sequence of parameters* $_n$ *2* $[0;1]$*, (*$n = 1;2;:::;N$*) and the Cauchy problem de ned in (5.1)-(5.2). The discrete formalization of (5.1)-(5.2) by the ATM has the following form*

$$y_n = y_{n\ 1} + h_n(1 \quad _n)f(t_{n\ 1};y_{n\ 1}) + h_{n\ n}f(t_n;y_n);\ \ n = 1;2;:::;N; \tag{5.5}$$

$$y_0 = u_0: \tag{5.6}$$

Hence, $_n$ *2* $[0;1]$ are xed parameters for all $n = 1;2;:::;N$ 1 and it de nes for $_n = 0$ (for all n) explicit, otherwise implicit method. This methods are usually used for sti systems the cases $_n = 0{:}5$ for all n trapezoidal rule and $_n = 1$ for all n backward Euler are of practical interest, for non-sti problems we can also consider $_n = 0$ for all n explicit Euler.

The main idea of this approach is the approximation of the solution of the discretized Cauchy problems (5.5)-(5.6) by using di erent numerical schemes (implicit, explicit, IMEX, one-step, multi-step etc.) with varying step-sizes. It has bene ts e.g. for the numerical solution of problems with non-smooth solutions.

Let us de ne the local truncation error for the ATM. We suppose that function f is su ciently smooth. The local truncation error $^{(\ )}_n$ for the ATM can be de ned as

$$\overset{(\ )}{}_n = (1 \quad {}_n)\ \overset{(0)}{}_n + {}_n\ \overset{(1)}{}_n \tag{5.7}$$

where

$$\overset{(1)}{}_n = \frac{u(t_n) \quad u(t_n\ {}_1)}{h_n} + f(t_n; u(t_n)); \quad \overset{(0)}{}_n = \frac{u(t_n) \quad u(t_n\ {}_1)}{h_n} + f(t_n\ {}_1; u(t_n\ {}_1))$$

and $u(t)$ stands for the solution of the problem (5.1)-(5.2).

By expanding $u(t_n)$ and $u(t_n\ {}_1)$ into the Taylor series around the point $t = t_n\ {}_1$ and $t = t_n$, respectively, we get for error the following

$$\overset{(\ )}{}_n = \frac{h_n}{2} \quad {}_n u''(t_n) \quad (1 \quad {}_n) u''(t_n\ {}_1) + \frac{h_n^2}{6} \left[(1 \quad {}_n) u'''(\ \overset{(1)}{}_n) \quad {}_n u'''(\ \overset{(0)}{}_n) \right] \tag{5.8}$$

where $\overset{(1)}{}_n$ and $\overset{(0)}{}_n$ are some constants de ned from the Taylor series. By expanding again $u''(t_n)$ into the Taylor series around the point $t = t_n\ {}_1$, for the local approximation error we get the following

$$\overset{(\ )}{}_n = C_n^{(1)} h_n + C_n^{(2)} h_n^2 \tag{5.9}$$

where

$$C_n^{(1)} = \frac{2 \ {}_n \quad 1}{2} u''(t_n\ {}_1); \ C_n^{(2)} = \frac{1}{6}(1 \quad {}_n) u'''(\ \overset{(1)}{}_n) \quad \frac{1}{6}\ {}_n u'''(\ \overset{(0)}{}_n) + \frac{1}{2} u'''(\ \overset{(2)}{}_n):$$

To de ne the order of the numerical method we estimate moreover the truncation error using (5.4) as follows

$$\overset{(\ )}{}_n \qquad C_n^{(1)}\ h_n + C_n^{(2)}\ h_n^2 \quad \frac{2 \ {}_n \quad 1}{2} M_2 C h + \frac{2}{3} M_3 C h^2 \tag{5.10}$$

where

$$M_2 = max_n\ u''(t_n)\ ; \ M_3 = max_n\ u'''(t_n)\ :$$

The order of a numerical method is de ned by the local truncation error. When $\overset{(\ )}{}_n(h) = O(h^{p+1})$ for all n then the method is called consistent of order p. This means that for both Euler methods the order of consistency is equal to one, while for the "pure" trapezoidal rule the order of consistency is equal to two.

However the consistency in itself does not guarantee the convergence of a numerical method, the stability is also required. Our aim is to give an easy and elementary prove for the convergence

of the general ATM. Moreover we give the expression for the stability constant of the method, as well.

5.2 Convergence and applications

In this section we use a sequence of meshes $!_h$ and we de ne the numerical solution at some xed point $t^? \ 2 \ (0; T)$ to the Cauchy problem (5.1)-(5.2) for the general ATM de ned in (5.5)-(5.6) with

$$h_1 + h_2 + \quad + h_N \ = t^?:$$

The usual way of proving the convergence of the single step -method is to show the zero-stability, by using its rst characteristic polynomial. The proof of it can be found in [19], [20]. However, the proof is complex and needs several auxiliary statements.

In the sequel, we give an elementary proof of the convergence by using the following lemma.

Lemma 5.2 *Let* $a_n > 0$, $b_n \quad 0$ *for all* $n = 1; 2; : : :$, *and* s_n *be such numbers that the inequalities*

$$js_n j \quad a_n js_{n \ 1} j + b_n; \ \ n = 1; 2; : : : \tag{5.11}$$

hold. Then the estimate

$$js_n j \quad \left(\prod_{l=1} a_l \right) \left(js_0 j + \sum_{j=1} b_j \left(\prod_{k=1} \frac{1}{a_k} \right) \right); \ \ n = 1; 2; : : : \tag{5.12}$$

is valid.

Proof. By using induction, we can readily verify the statement. Indeed, for $n = 1$ in (5.12) is clearly valid. Now, under the that (5.12) holds for $n \quad 1$, from (5.11) we have

$$\begin{aligned} js_n j &\quad \left(\prod_{l=1} a_l \right) \left(js_0 j + \sum_{j=1}^{n-1} b_j \left(\prod_{k=1} \frac{1}{a_k} \right) \right) + b_n \\ &= \left(\prod_{l=1} a_l \right) \left(js_0 j + \left(\sum_{j=1} b_j \left(\prod_{k=1} \frac{1}{a_k} \right) \right) \quad b_n \left(\prod_{k=1} \frac{1}{a_k} \right) \right) + b_n \\ &= \left(\prod_{l=1} a_l \right) \left(js_0 j + \sum_{j=1} b_j \left(\prod_{k=1} \frac{1}{a_k} \right) \right) \quad b_n + b_n \end{aligned}$$

which yields the statement.

With our notations the form of inequality (5.12) can be rewritten into the following simpler form:

$$s_n \quad js_0j \prod_{l=1}^{!} a_l + \sum_{j=1}^{} b_j @ \prod_{l=j+1}^{} a_l A \quad \text{for all } n: \tag{5.13}$$

Remark 5.3 *If* $a_n \quad a$ *and* $b_n \quad b$ *for all* $n = 1;2;:::$, *then, according to (5.12), we have*

$$js_nj \quad a^n js_0j + b\frac{a^n \quad 1}{a \quad 1};\ \ n = 1;2;::: \tag{5.14}$$

inequality (c.f. [21]).

Conclusion 5.4 *If* $a_k \quad 1$, *then*

$$\prod_{k=1}^{i} \frac{1}{a_k} \quad \frac{1}{a_j}$$

holds which implies the inequality

$$js_nj \quad \prod_{l=1}^{!} a_l \quad 4js_0j + \sum_{j=1}^{} b_j \frac{1}{a_j} 5;\ \ n = 1;2;::: \tag{5.15}$$

Remark 5.5 *If* $a_n \quad a \quad 1$ *and* $b_n \quad b$ *for all* $n = 1;2;:::$, *then (5.14) implies the inequality* (c.f.[21])

$$js_nj \quad a^n js_0j + na^n \ ^1b;\ \ n = 0;1;:::$$

In the following, we consider the global error $e_n = u(t_n) \quad y_n$ at the mesh-point $t = t_n$. We get the recursion in the form

$$e_n = e_n \ _1 + h_n \ ^{(\ )}_n + h_n g_n; \tag{5.16}$$

where $^{(\ )}_n$ is de ned in (5.7) and

$$g_n = \ _n [f(t_n;u(t_n)) \quad f(t_n;y_n)] + (1 \quad \ _n)[f(t_n \ _1;u(t_n \ _1)) \quad f(t_n \ _1;y_n \ _1)]: \tag{5.17}$$

Hence, using the Lipschitz property (5.3) and the estimations (5.10) and (5.16), we get

$$je_nj \quad je_n \ _1j + h_n^2 jC_n^{(1)}j + h_n^3 jC_n^{(2)}j + h_n \ _n Lje_nj + h_n(1 \quad \ _n)Lje_n \ _1j \tag{5.18}$$

for any $n = 1;2;:::;N$. After re-arrangement of (5.18), we obtain

$$|e_n| \quad 1 + \frac{h_n L}{1 \quad h_{n\ n} L} |e_{n\ 1}| + \frac{h_n^2}{1 \quad h_{n\ n} L} \quad |C_n^{(1)}| + h_n |C_n^{(2)}| \quad : \tag{5.19}$$

Let us denote

$$a_n = 1 + \quad {}_n h_n \text{ where } \quad {}_n = \frac{L}{1 \quad h_{n\ n} L} \tag{5.20}$$

and

$$b_n = \quad {}_n h_n^2 \text{ where } \quad {}_n = \frac{|C_n^{(1)}| + h_n |C_n^{(2)}|}{1 \quad h_{n\ n} L}. \tag{5.21}$$

Then, by choosing a_n and b_n according to (5.20)-(5.21), and using the inequality $1 + x \quad exp(x)$ for $x \quad 0$, Conclusion 5.4 implies the estimate

$$|e_n| \quad \left(\prod_{l=1} e^{\ l h_l} \right) \left(4|e_0| + \sum_{j=1} {}_j h_j^2 5 \right) \quad e^{\ max \sum_{l=1}^{n} h_l} \left(4|e_0| + {}_{max} \sum_{j=1} h_j^2 5 \right); \tag{5.22}$$

where

$${}_j = \frac{{}_j}{1 + \quad {}_j h_j}; \quad {}_{max} = max_j \quad {}_j; \quad {}_{max} = max_j \quad {}_j : \tag{5.23}$$

Let $t^? \ 2 \ (0; T)$ xed point, $h := \frac{t^?}{n}$. Assuming (5.4) for all $n = 1; 2; : : :$ we get

$$\sum_{j=1} h_j \quad Ct^? h: \tag{5.24}$$

The next step is the estimation of ${}_{max}$ and ${}_{max}$. We have

$${}_{max} \quad \frac{{}_{max}}{1 + \quad {}_{min}} \qquad {}_{max} \quad \frac{\frac{1}{2} max_n (2 \quad {}_n \quad 1) M_2 + Ch \frac{2}{3} M_3}{1 \quad Ch \quad max_n (\ {}_n) L}; \qquad$$

$${}_{max} = \frac{L}{1 \quad Ch \quad max_n \quad {}_n L}: \tag{5.25}$$

Hence, by the notation ${}_{max} := max_n (\ {}_n)$, (5.23),(5.24) and (5.25) implies the relation

$$|e_n| \quad exp \quad \frac{L}{1 \quad Ch \ {}_{max}} t^? \quad (|e_0| + Cht^? \ {}_{max}); \ n = 1; 2; : : : : \tag{5.26}$$

Because $e_0 = 0$, the relation (5.26) results in the estimate

$$|e_n| \quad \exp\left(\frac{L}{1 \quad Ch}\right)_{max} t^{?} \quad Cht^{?}{}_{max}: \tag{5.27}$$

Theorem 5.6 *When n tends to in nity and* (5.4) *holds, then the numerical method (5.5)-(5.6) is convergent at any xed point* $t^{?} \in (0;T)$ *in rst order, assuming that* $e_0 = 0$ *or* $e_0(h) = O(h)$ *is valid.*

Proof. As a consequence of assumption $h \to 0$, hence for the right side of (5.27) we have

$$\lim_{h \to 0} \exp\left(\frac{L}{1 \quad Ch}\right)_{max} t^{?} \quad = \exp(Lt^{?})$$

and

$$\lim_{h \to 0} \quad _{max} = \frac{\#_{max}}{2} M_2; \text{ where } \#_{max} := max_n|2 \quad _n \quad 1|$$

therefore

$$|e_n| \quad \exp(Lt^{?})\frac{\#_{max}}{2} M_2 = Const \quad h \tag{5.28}$$

which yields the rst order convergence.

Remark 5.7 *Using the statement of Theorem 5.6 for the special case, i.e., to the pure explicit and implicit Euler schemes when for any* $n = 1;2;:::$ $_n \quad 0$ *or* $_n \quad 1$*, respectively, and* $h_n \quad h$*, we re-obtain the classical result.*

Consequence 5.8 *In case of* $_n \quad 0{:}5$ *for* $h_n \quad h$ *for any* $n = 1;2;:::$ *(trapezoidal formula) the convergence order is equal to two, and the stability constant is equal to* $(2{=}3)CM_3$*, since in estimation (5.28) the value of* $\#_{max}$ *is equal to zero.*

As a conclusion we can say, that ATM can be used e ectively on ODE-s. In the following chapters we will apply ATM on PIDE systems similarly to the classical -method described in Section 4.2.

Chapter 6

Improvement of the discretization algorithm

6.1 Combination of sequential splitting and alternant- -method

After we have introduced the population-migration epidemic spread model in Chapter 3 and the ATM in Chapter 5, our aim is to improve the -method described in Chapter 4 by using the combination of sequential splitting and ATM (called in the further SS-ATM).

Let us de ne $^{(l)}_{j}{}^{n;i} := {}_{j}(t_n; x_i)$ for $j = 1; 2$, where l denotes the solution of l-th sub-problem in the sequential splitting algorithm and the time and spatial step sizes are denoted by and h, respectively. We will use the notations de ned in (4.1) and (4.4).

Problem 1 (linear part)

Main equation

$$\frac{^{(1)}_{j}{}^{n;i} \quad ^{(1)}_{j}{}^{n \quad 1;i}}{} = {}_{n}\,{}^{(1)}_{j}{}^{n \quad 1;i}A_j + C_j\frac{h}{2}\,{}^{(1)}_{j}{}^{n \quad 1;i} + {}^{(1)}_{j}{}^{n \quad 1;i \quad 1} + {}^{(1)}_{j}{}^{n \quad 1;i}{}_{j}B_j + f_j^{n \quad 1;i} +$$

$$+ (1 \quad {}_{n})\,{}^{(1)}_{j}{}^{n;i}A_j + C_j\,\frac{h}{2}\,{}^{(1)}_{j}{}^{n;i} + {}^{(1)}_{j}{}^{n;i \quad 1} + {}^{(1)}_{j}{}^{n;i}{}_{j}B_j + f_j^{n;i} \qquad (6.1)$$

$$(i = 1; 2; : : : ; N_x; \quad n = 1; 2; : : : ; N_t + 1; \quad {}_{n} \; 2 \; [0; 1])$$

Initial conditions

$$^{(1)}_{j}{}^{0;i} = {}^{(1)}_{j;0}{}^{i} \quad (i = 1; 2; : : : ; N_x) \qquad (6.2)$$

Boundary conditions

$$\frac{^{(1)}_{j}{}^{n;1} \quad ^{(1)}_{j}{}^{n;0}}{h} = K^n_{j;1}; \quad \frac{^{(1)}_{j}{}^{n;N_x} \quad ^{(1)}_{j}{}^{n;N_x \quad 1}}{h} = K^n_{j;2} \quad (n = 1; 2; : : : ; N_t + 1) \qquad (6.3)$$

Problem 2 (nonlinear part)

Main equation

$$\frac{{}^{(2)}_{j}{}^{n;i} - {}^{(2)}_{j}{}^{n-1;i}}{} = \left[{}_{n}\,{}^{(2)}_{j}{}^{n-1;i} + {}^{(2)}_{j}{}^{n-1;i} D_j + (1 - {}_{n})\,{}^{(2)}_{j}{}^{n;i} + {}^{(2)}_{j}{}^{n;i} D_j \right] \tag{6.4}$$

$$(i = 1; 2; \ldots; N_x; \quad n = 1; 2; \ldots; N_t + 1; \quad {}_{n} \in [0; 1])$$

Initial conditions

$${}^{(2)}_{j}{}^{0;i} = {}^{(1)}_{j}{}^{1;i} \qquad (i = 1; 2; \ldots; N_x) \tag{6.5}$$

Next we develop a test system to measure the accuracy of the SS-ATM defined above in (6.1)-(6.5). Let us choose as exact solutions the following functions

$${}_1(x; t) = e^{t} \sin(x); \quad {}_2(x; t) = e^{x} \cos(t) \tag{6.6}$$

on the $[0; \ ]$ space and $[0; 1]$ time intervals, which yield the following form of system (4.3)

$$\begin{cases} \dfrac{\partial {}_1}{\partial t} = 0.01\,{}_1 - 0.01\,{}_2 + 0.002 \displaystyle\int_0^{} {}_1 dx + 0.04\,{}_1\,{}_2 + f_1(x; t) \\ \dfrac{\partial {}_2}{\partial t} = -0.02\,{}_2 + 0.01\,{}_1 + 0.002 \displaystyle\int_0^{} {}_2 dx - 0.04\,{}_1\,{}_2 + f_2(x; t) \\ {}_1(x; 0) = \sin(x); \quad {}_2(x; 0) = e^{x}; \quad x \in [0; \ ] \\ \dfrac{\partial {}_1}{\partial x} = e^{t}; \quad \dfrac{\partial {}_2}{\partial x} = e^{x} \cos(t); \quad x = 0 \text{ or } \ ; \quad t \in [0; 1] \end{cases} \tag{6.7}$$

next to the parameter setting

$$A_1 = 0.01; \quad B_1 = -0.01; \quad C_1 = 0.002; \quad D_1 = 0.04$$

$$A_2 = -0.02; \quad B_2 = 0.01; \quad C_2 = 0.0001; \quad D_2 = -0.04.$$

Substituting the exact solutions defined in (6.6) into the system (6.7), after some calculations we can determine functions f_1 and f_2, as well, which provide us the following results

$$\begin{aligned} f_1(x; t) &= \cos(t) e^{x} (1 - 4e^{t} \sin(x)) \\ f_2(x; t) &= e^{x} (2\cos(t) - \sin(t)) - e^{t} \sin(x)(1 - 4e^{x} \cos(t)) - 2\cos(t)(e^{(-2)} - 1). \end{aligned} \tag{6.8}$$

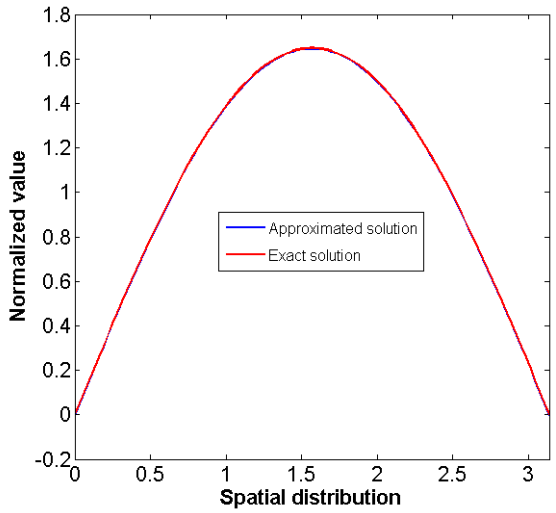


Figure 6.1: Exact and approximated solution of system (6.7) for $_1$ by using SS-ATM at t = 0:5.

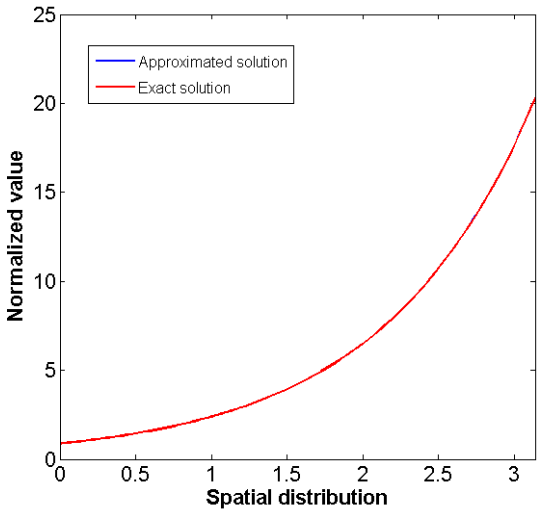


Figure 6.2: Exact and approximated solution of system (6.7) for $_2$ by using SS-ATM at t = 0:5.

Using the SS-ATM algorithm de ned in (6.1)-(6.5), we can implement the exact and the approximated results (see in Figure 6.1 and 6.2) and they absolute errors measured in the discrete l_2 norm (see in Figure 6.3).

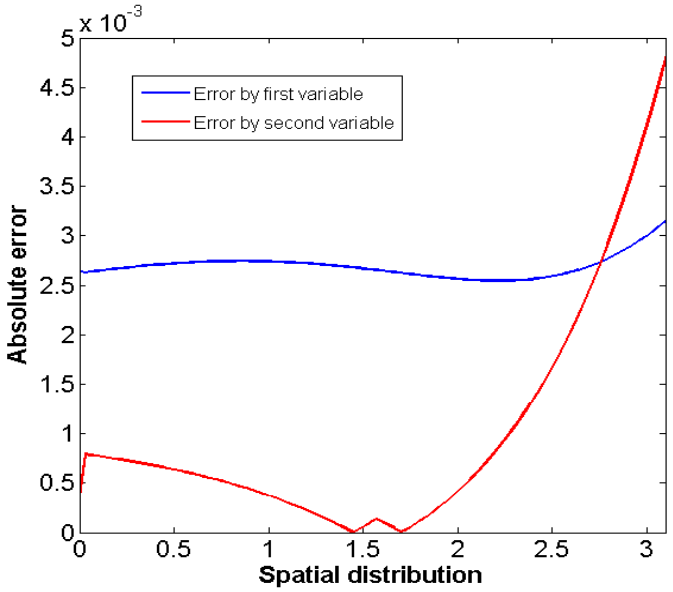


Figure 6.3: Absolute error of system (6.7) for $_1$ and $_2$ by using SS-ATM at t = 0:5.

According to the gures, we can conclude, that SS-ATM can apply e ectively on the test system. The question is only the di erence between di erent numerical schemes in sense of accuracy and running time. In the next section we are going to answer this question by comparing the classical explicit-; implicit-Euler method, ATM and SS-ATM.

6.2 Comparison of numerical schemes

To establish the accuracy and running time of the approximation scheme de ned in (6.1)-(6.5) we test some other numerical model on the test system in (4.5). By these kind of models we need to discretize according to the time and space variables, similarly to the ATM. As spatial discretization by the integral we will use the trapezoidal quadrature rule and by time discretization algorithms, the following schemes have been used: Explicit-Euler method (EEM), Implicit-Euler method (IEM), Alternant- $_n$ method (ATM) and Sequential splitting with ATM (SS-ATM).

Table 6.1 summarizes the running times and average errors of the di erent approximation methods in space and time, where the error was measured in the discrete $_1$ norm. The spatial step size has been chosen in every case as 0.01 and the sequential splitting has only 1 microscopical step, because the results already re ect the e ectiveness of operator splitting.

Time step size	EEM	IEM	ATM	SS-ATM
	Running time (sec)			
0.1	0.001471	0.002592	0.004605	0.002323
0.01	0.015628	0.025739	0.027065	0.024813
0.001	0.133629	0.255513	0.232288	0.241891
0.0001	1.433470	2.525491	2.248102	2.354832
	Absolute average error			
0.1	0.0926	0.0863	0.0903	0.0718
0.01	0.0103	0.0097	0.0101	0.0082
0.001	0.0021	0.0020	0.0021	0.0019
0.0001	0.00187967	0.00187961	0.00188135	0.00186959

Table 6.1: Comparison the running time between numerical schemes.

According to Table 6.1 one can see that EEM is the fastest approximation however it has the largest average error (as it was expected). IEM resulted more accurate solution, but its running time was almost double of the running time of EEM. On the other hand, the ATM can taken as some kind of average of EEM and IEM because its error is between of them and also (by very small time step sizes) its running time, i.e. the speed-up property of ATM can be applied e ectively. The main and most useful result is that the SS-ATM has the lowest average error in absolute value, thus one can see that the operator splitting algorithms can be used e ectively by PIDEs, as well.

From this point we hypothesise that these results re ect the e ectiveness of SS-ATM applied on the original population migration system de ned in (3.8)-(3.11). Accept this assumption, in the last chapter we are going to implement the approximated result of the continuous model de ned in (3.8)-(3.11), and we further assume, that the results are synchronised with the reality.

Chapter 7

Numerical test on the complex Ebola model

7.1 Numerical approximation

In this chapter we focus on the results of the numerical approximation applied on the Ebola epidemic spread model de ned in (3.8)-(3.11). Firstly we describe the algorithm of the SS-ATM, de ned in (6.1)-(6.5), on the generalized epidemic model in (4.3) by using notations in (4.1), as follows:

Problem 1 (linear part)
Main equation

$$\frac{{}^{(1)}_{j}{}^{n;i} - {}^{(1)}_{j}{}^{n\ 1;i}}{} = {}_{n}\ F_j\ {}^{(1)}_{j}{}^{n\ 1;i} + G_j\ {}^{(1)}\sim_{j}{}^{n\ 1;i} + f_j^{n\ 1;i} +$$

$$+ (1\ {}_{n})\ F_j\ {}^{(1)}_{j}{}^{n;i} + G_j\ {}^{(1)}\sim_{j}{}^{n;i} + f_j^{n;i} \qquad (7.1)$$

$$(i = 1; 2; : : : ; N_x\ \ 1; \quad n = 1; 2; : : : ; N_t; \quad {}_{n}\ 2\ [0; 1])$$

Initial conditions

$${}^{(1)}_{j}{}^{0;i} = {}^{(1)}_{j;0} \quad (i = 1; 2; : : : ; N_x\ \ 1) \qquad (7.2)$$

Boundary conditions

$$\frac{{}^{(1)}_{j}{}^{n;1} - {}^{(1)}_{j}{}^{n;0}}{h} = K^{n}_{j;1}; \quad \frac{{}^{(1)}_{j}{}^{n;N_x} - {}^{(1)}_{j}{}^{n;N_x\ 1}}{h} = K^{n}_{j;2} \quad (n = 1; 2; : : : ; N_t) \qquad (7.3)$$

Problem 2 (nonlinear part)

Main equation

$$\frac{{}^{(2)}_{j}{}^{n;i} \quad {}^{(2)}_{j}{}^{n \quad 1;i}}{} = {}_{n}\hbar H_j \quad {}^{(2)}\sim \; ;{}^{(2)}\sim i^{n \quad 1;j} + (1 \quad {}_{n})\hbar H_j \quad {}^{(2)}\sim \; ;{}^{(2)}\sim i^{n;j} \tag{7.4}$$

$$(i = 1; 2; : : : ; N_x \quad 1; \quad n = 1; 2; : : : ; N_t; \quad {}_{n} \; 2 \; [0; 1])$$

Initial conditions

$${}^{(2)}_{j}{}^{0;i} = {}^{(1)}_{j}{}^{1;i} \qquad (i = 1; 2; : : : ; N_x \quad 1) \tag{7.5}$$

Let us apply now the following substitutions. The subscript by the operators denotes the subgroups, the functions ${}_j$ are taken for set $f S; E; I; C; R; Q; V g$ for $j = 1; 2; : : : ; 7$ respectively. Furthermore $\sim_j$ will be denoted by $S; E; I; C; R; Q$ and V for all j. With all this in mind we can de ne the operators of self dependency:

$$\begin{cases}
(F_S(S))(x;t) = (\quad (x;t) \quad {}_S(x;t) \quad v_e(x) + \quad (x;t))\, S(x;t) + \quad \int v(x;y)S(y;t)dy \\
(F_E(E))(x;t) = (\quad (x;t) \quad {}_E(x;t) \quad v_e(x))\, E(x;t) + \quad \int v(x;y)E(y;t)dy \\
(F_I(I))(x;t) = (\quad "(x;t) \quad {}_I(x;t) \quad (x;t) \quad {}_I(x;t) \quad v_e(x))\, I(x;t) + \\
\qquad + \quad \int v(x;y)I(y;t)dy \\
(F_C(C))(x;t) = (\quad (x;t) \quad {}_C(x;t) \quad v_e(x))\, C(x;t) + \quad \int v(x;y)C(y;t)dy \\
(F_R(R))(x;t) = (\quad (x;t) \quad {}_R(x;t) \quad v_e(x))\, R(x;t) + \quad \int v(x;y)R(y;t)dy \\
(F_Q(Q))(x;t) = (\quad ' (x;t) \quad {}_Q(x;t) \quad {}_Q(x;t) \quad v_e(x))\, Q(x;t) + \quad \int v(x;y)Q(y;t)dy \\
(F_R(R))(x;t) = (\quad {}_V(x;t) \quad v_e(x))\, V(x;t) + \quad \int v(x;y)V(y;t)dy
\end{cases} \tag{7.6}$$

operators of dependency of other groups:

$$\begin{cases} G_S(S)\ \ (x;t) = \quad (x;t)R(x;t) + \quad (x;t)\,(E(x;t) + I(x;t) + C(x;t)) + \\ \qquad\qquad\qquad + \quad (R(x;t) + Q(x;t) + V(x;t)) \\ G_E(E)\ \ (x;t) = 0 \\ G_I(I)\ \ (x;t) = \quad (x;t)E(x;t) \\ G_C(C)\ \ (x;t) = \ "(x;t)I(x;t) + \ '\ (x;t)Q(x;t) \\ G_R(R)\ \ (x;t) = \quad (x;t)C(x;t) \\ G_Q(Q)\ \ (x;t) = \quad (x;t)I(x;t) \\ G_V(V)\ \ (x;t) = \quad (x;t)S(x;t) \end{cases} \tag{7.7}$$

and nally the operators of nonlinear dependency:

$$\begin{cases} hH_S(\sim);\sim i(x;t) = \quad \frac{\ _I(x;t)}{N(x;t)}I(x;t) + \frac{\ _C(x;t)}{N(x;t)}C(x;t)\ \ \ S(x;t) \\ hH_E(\sim);\sim i(x;t) = \ \frac{\ _I(x;t)}{N(x;t)}I(x;t) + \frac{\ _C(x;t)}{N(x;t)}C(x;t)\ \ \ S(x;t) \end{cases} \tag{7.8}$$

and for the others the nonlinear operator is equal to 0.We mention at this point that our model does not include any source function, thus f_j are taken as zero for all j.

Using declarations in (7.6)-(7.8) and algorithm in (7.1)-(7.5) we can begin the numerical approximation of the model. However we still need to estimate the unknown parameters.

7.2 Parameter estimation and analysis of results

Our aim is to give a short introduction into the parameter estimations by PIDEs of epidemic spread models. We would like to avoid the fully description of parameter estimation because that would be out of the range of this thesis. Thus we mention the basic data, their references and sources.

The West African Ebola virus epidemic (2013 2016) was the most widespread outbreak of Ebola virus disease (EVD) in historycausing major loss of life and socioeconomic disruption in

the region, mainly in the countries of Guinea, Liberia, and Sierra Leone. The first cases were recorded in Guinea in December 2013; later, the disease spread to neighboring Liberia and Sierra Leone [22] with minor outbreaks occurring elsewhere. It has caused significant mortality, with the case fatality rate reported at slightly above 70%, while the rate among hospitalized patients was 57 59% [23].

The number of cases peaked in October 2014 and then began to decline gradually, following the commitment of substantial international resources. As of 8 May 2016, the World Health Organization (WHO) and respective governments reported a total of 28,616 suspected cases and 11,310 deaths 39.5% [24], though the WHO believes that this substantially understates the magnitude of the outbreak [25].

On 29 March 2016, the WHO terminated the Public Health Emergency of International Concern status of the outbreak [26]. Subsequent flare-ups occurred; the last was declared over on 9 June 2016, 42 days after the last case tested negative on 28 April 2016 in Monrovia [27].

The outbreak left about 17,000 survivors of the disease, many of whom report post-recovery symptoms termed post-Ebola syndrome, often severe enough to require medical care for months or even years. Figure 7.1 shows well the distribution of infected individuals.

Figure 7.1: Distribution of infected individuals.

On Figure 7.2 are implemented the total cases agregated to timeline. In this thesis we focus on the outbreak of Ebola in Guinea. Thus, on Figure 7.3 we can see this data specified to Guinea with the number of total deaths.

Figure 7.2: Total infected cases agregated to timeline.

Figure 7.3: Total infected and total death cases in Guinea.

We assume now that all per-capita rates and initial conditions are constants in time and space. The total initial population size of Guinea, i.e. N_0 is supposed to be 10628972 according to [28]. According to Figure7.3, the initial number of infected individuals with clinical symptoms, i.e. I_0 is equal to 37500. For the shake of better visibility we will normalize the parameters in further according to the whole population size (N). Other parameters are also estimated similarly, according to the above mentioned which are contained by Tables in Appendix A.

Now we are able to approximate the system (3.9) with initial (3.8) and boundary conditions (3.10)-(3.11) next to the parameter settings declared in Table A, based on the numerical approximation scheme de ned in (7.1)-(7.5) by using operators in (7.6)-(7.8).

For simplicity in this work we analyze the 1 dimensional system on the $[0L]$ space and $[0T]$ time intervals. Furthermore all of time and space dependent parameter functions supposed to be used as constant functions. The used parameters are summarized in Tables in Appendix A.

We apply the ATM numerical scheme on the system and we implement the splitted solution solved by sequential splitting. The examined time and space intervals are chosen as; $[0]$ and $[0; 1]$. Let's consider a mesh with micro time step size , macro time step size and spatial step

size h chosen as 0.01, 0.1 and 0.01, respectively. With all this in mind we implement the results on Figure 7.4 where the different colors represent different locations (green, blue, red).

Figure 7.4: Solution functions of various groups and total population, where the different colors represent different locations (green, blue, red)

The right-bottom part of Figure 7.4 shows that the number of the whole population decreases at the beginning of analyzed time interval because of the epidemic and the emigration rate. Later this number behaves invertible because the birth and immigration rate overtake the death rate. We can obtain the same behaviour by susceptibles on the first subplot with faster manner. It can be concluded that the population will not extinct by the used parameter settings. On the one part this is because the initial population size was relatively high, on the other hand we have been assumed respectable small number of infected individuals. Top-middle part of Figure 7.4 implements the numerical behaviour of sub-populations after infection. Function of infected individuals shows a strongly decreasing behaviour because of the very small reinfection-rate ( ) and the really big mortality rate ( ). The compartments of individuals immediately before (E), after (C) infection and in quarantines (Q) are not surprising. At the very beginning of the disease they are increasing however after the critical period the number of individuals inside these two groups converges to zero such as the number of infected people. Size of group of recovered and vaccinated individuals from epidemic shows a strongly increasing behaviour in contrast with infected or susceptible people since the getting out rate, such as it was explained before, is small and every individuals survived the virus. Obviously the increasing speed is high only at the beginning of the epidemic.

Chapter 8

Conclusion and outlook

In this work we gave a short introduction for the mathematical modeling of Ebola epidemic spread and we produced some new results with respect to the numerical approximations. The main aim of this work was to develop an extended epidemic model of Ebola in form of partial-integral-di erential equations (PIDEs) by using time and space dependency, furthermore we have developed the general PIDEs in continuous and in discretized form, as well.

Additionally, we determined that the sequential splitting algorithm based on the alternant- $_n$ scheme is e ective to approximate the solution numerically, since it has the best running time and lowest average error measured in discrete L_2 norm. The main conclusion is that the operator splitting technique can be applied easily to extend the existing model by other in uential factors and sub-groups such as quarantines, vaccination or the population migration factor.

As further work we can extend the model by time-delayed infection rates or we can classify the individuals by ages or sexual attitudes, which strongly a ect the spread of the virus. As further numerical analysis, the convergence of the numerical model, investigation of the properties and solutions of di erent operator splitting techniques or numerical schemes can be interesting and could provide further informations, as well.

Finally, we can conclude that the accurate modelling of disease spread of Ebola and other viruses are possible by using our generalized model, which can be used to give some preventative suggestions to predict the virus and perhaps rescue thousands of people.

Appendix A

Parameters

Parameters	Meaning	Normalized estimation
N_0	Initial number of individuals	0.4676
S_0	Initial suspectibles	0.3676
E_0	Initial latents	0.1000
M_0	Other initial numbers	0
	Birth rate	0.0548
	Natural death rates	0.0157
$_I$	Infection rate by I	0.7000
$_C$	Infection rate by C	0.5000
	Vaccination rate	0.00002
	Loss of immunity rate	0.0002
	Loss of latent period rate	0.95
"	Loss of dangerous infection rate	0.75
$_I$	Death rate of I caused by Ebola	0.75
$_Q$	Death rate of Q caused by Ebola	0.8
	Quarantine rate	0.24
'	Recovery rate from quarantine	0.45
	Recovery rate from C	0.9
v	Migration rate	0.25
v_e	Emigration rate	0.04
m	Hollow point of epidemic	2.5
s	Flux constant of S	10
e	Flux constant of E	1
i	Flux constant of I	2
c	Flux constant of C	3
r	Flux constant of R	4
q	Flux constant of Q	5
v	Flux constant of V	1

Table A.1: Estimated parameters for numerical calculations

Bibliography

[1] WHO Ebola Response Team, Situation Report Ebola Virus Disease, 10 June 2016.

[2] http://edition.cnn.com/2015/10/15/health/who-ebola-report/

[3] http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/

[4] https://sphcm.med.unsw.edu.au/infectious-diseases-blog/reinfection-ebola-%E2%80%93-it--possible-and-should-health-worker-survivors-use-ppe

[5] Glynn J.R., Age-speci c incidence of Ebola virus disease, The Lancet, 386 (2015), 432.

[6] http://www.who.int/features/2015/guinea-ebola-vaccine/en/

[7] Capasso V., Mathematical Structures of Epidemic Systems, Lecture Notes in Biomathematics, Springer 97, 1993.

[8] Dietz K., Hadeler K.P., Epidemiological models for sexually transmitted diseases. J. Math. Biol. 26 (1988), 1-25.

[9] Capasso V., Mathematical modelling of transmission mechanisms of infectious diseases. 1st European Conference on Math. Appl. Biology and Medicine, 1992.

[10] Kermack W.O., McKendrick A.G., Contributions to the mathematical theory of epidemics. Part I, Proc. Roy. Soc., A, 115 (1927), 700-721.

[11] Hamer W.H., Epidemic diseases in England. Lancet 1 (1906), 733-739.

[12] Wilson E.B., Worcester J., The law of mass action in epidemiology. Part I, Proc. Nat. Acad. Sci., 31 (1945), 24-34.

[13] Havasi A., Bartholy J., Farago I., Splitting method and its application an air pollution modelling, Idojaras, 105 (1) (2001), 39-58.

[14] Botchev M.A., Farago I., Horvath R., Application of operator splitting to the Maxwell equations including a source term, Applied Numerical Mathematics, 59 (1) (2009), 522{541.

[15] Kriston A., Inzelt Gy., Farago I., Szabo, T., Simulation of the transient behavior of fuel cells by using operator splitting techniques for real-time applications, Computers & Chemical Engineering, 34 (3) (2010), 339 - 348.

[16] Csomos P., Farago I., Havasi A., Weighted sequential splitting and their analysis, Computers & Mathematics with Applications, 50 (7) (2005), 1017 - 1031.

[17] Legrand J., Grais R.F., Boelle P.Y., Understanding the dynamics of Ebola epidemics, Epidemiology and Infection, 135 (4) (2007), 610-621.

[18] Cui S., Bai M., Mathematical analysis of population migration and its e ects to spread of epidemics, Discrete and Continuous Dynamical Systems, 204 (9) (2015), 2819.

[19] Isaacson E., Keller H. B., Analysis of numerical methods, Wiley, New York, 1966.

[20] Suli E., Numerical solution of ordinary di erential equations, Oxford, 2010.

[21] Farago I., Convergence and stability constant of the theta-method, Application of Mathematics, 42-51, 2013.

[22] WHO Ebola Response Team, Ebola virus disease in West Africa the rst 9 months of the epidemic and forward projections. New England Journal of Medicine. 371: 148195. 23 September 2014.

[23] WHO Ebola Response Team, Ebola Situation report. Ebola data and statistics. 12 January 2015.

[24] WHO Ebola Response Team, Ebola data and statistics. 9 June 2016.

[25] Worl J., New Ebola Cases Could Hit 10,000 Per Week. Time.com. Time. 2014.

[26] WHO Ebola Response Team, WHO Director-General briefs media on outcome of Ebola Emergency Committee.

[27] WHO Ebola Response Team, Situation Report Ebola Virus Disease. 10 June 2016.

[28] https://hu.wikipedia.org/wiki/Guinea [29] Coville J., On a simple criterion for the existence of a principal eigenfunction of some nonlocal operators, J. Di . Equa., 249 (2010), 2921-2953.

[30] Farkas Z., Development and mathematical analysis of a space dependent integro-di erential model for the spread of Ebola by using operator splitting, Annales Univ. Sci. Bp., Sect. Comp., 45 (2016), 135-156.

[31] Farago I., Farkas Z., Convergence of alternant theta-method with applications, Numerical Analysis and its Applications, NAA 2016 Lecture Notes in Computer Science, vol 10187, Springer, Cham.

[32] Farkas Z., Farago I., Kriston A., Pfrang A., Improvement of accuracy of multi-scale models of Li-ion batteries by applying operator splitting techniques (2016), Journal of Computational and Applied Mathematics, Volume 310, 59-79.

Declaration of Authorship

Név: Farkas László Zénó
ELTE Természettudományi Kar, szak: Alkalmazott matematikus
NEPTUN azonosító: RRRKWJ
Szakdolgozat címe: Development and Numerical Analysis of a Space and Time Dependent Model for the Spread of Ebola by using Operator Splitting Techniques

A szakdolgozat szerzőjeként fegyelmi felelősségem tudatában kijelentem, hogy a dolgozatom önálló munkám eredménye, saját szellemi termékem, abban a hivatkozások és idézések standard szabályait következetesen alkalmaztam, mások által írt részeket a megfelelő idézés nélkül nem használtam fel.

Budapest, 2017

_____

hallgató aláírása