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DEVELOPMENT AND MATHEMATICAL ANALYSIS OF A SPACE-DEPENDENT INTEGRO-DIFFERENTIAL MODEL FOR THE SPREAD OF EBOLA BY USING OPERATOR SPLITTING

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Abstract. 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 a feasible delivery system, the speed of producing the vaccine, a drug for Ebola or the effect of the migration so that we can optimize the eradication of the virus. In this work we develop a model to describe the dynamic of the virus in space and time and for this purpose the extended version of the SEIRS epidemic spread model is used in combination with extra carriers and other groups. Our aim is to extend this model by different influential factors, such as the population migration. This modification introduces space dependence into the system and transforms it into the form of partial differential equations. One way to combine the original system with the migration model is the operator splitting method, which allows us to solve the extra operators connected to each other by the appropriate initial conditions independently from the basic model. Thus we apply the sequential splitting method based on the classical explicit Euler scheme for the numerical analysis in order to predict the morphosis of the disease spreading and to give some preventative or amending suggestions.

Key words and phrases: Ebola, migration, numerical model, operator splitting, time discretization.
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1. Introduction and biological backgrounds

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 feasible delivery system, the speed of manufacturing of the vaccine or drug for Ebola so that we can optimize its eradication of it. 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 of the for people from them is a so called Zaire Ebola virus (ZEBOV). The first registered person with Ebola virus was the 44 years old teacher, Mabalo Lokela. The affection was caused perhaps by a reused unsterilized hollow needle. 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. The occurrence of the virus in natural environment and possible infections to people are not known. 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.

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 ZEBOV virus does not spread among airborne. It follows that it can only circulate among people by direct contact with infected blood or other body-fluids (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.

After infection, a latent period $(4 - 10)$ days is expected. After that the disease begins suddenly with flue-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 first symptoms, haemorrhagic fever stigmas emerge and the morality rate in this phase is approximately $70-80\%$, but in Africa this rate is higher.

Survivors might become fully recovered from the disease, however, the healing process can take a long time, as well, even weeks or months and the virus may be present for a good while in the body-fluids (for example in semen). A good counter example was written in an online article from October, 2015 about a recovered man who had after 9 and a half months still Ebola virus in his semen [1]. 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-influence 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 [2], not one official re-infected affair happened. For additional soothing a study was published by an other research documentation in 2014 [3] where it was shown that the organism of a totally recovered 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. At last it is worth mentioning that Ebola virus is an age specify infection, i.e. the disease progress takes different times by different age groups [7].

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 effective disposalt, the prevention of the infection has a central role in people's life. Diseased and necrolatry by Ebola are miasmatic by contact with body-fluids. 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 [2]. The effect of these was the development of a vaccine which was tested in Guinea where researchers experimented 100% successfulness by testing 7651 individuals [4].

At last we describe how this paper is organized. In Section 2 we introduce the used basic model of SEICR [6] and we define the basic notations. In Section 3 we extend the SEICR model by 3 various influential factors, namely quarantines, vaccination and vital dynamic with natural birth and mortality rate. The basic model of population migration is presented in Section 4 where the coupled system is developed, together with initial and boundary conditions. Section 5 is for getting acquainted with the numerical algorithm of the sequential splitting method. In this section we determine also the coupling procedure of the extended SEICR and the population migration model. In Section 6 we

define the general form of the partial-integral-differential equations (PIDEs) and we prove a statement about the qualitative properties of the discretized numerical model of it to. In the last section we do some numerical tests in order to say something about the effectiveness of the sequential splitting algorithm and about the behaviour of individuals in different subgroups within the population during the epidemic.

2. Basics of the model

In mathematical epidemic modeling there exist many structures for disease spreading. From these, in this work the $SEIR$-model is used as default model, e.g. [6], with extra carriers, denoted by C. For combining them, the $SEICR$-model was developed, where initials define the following arts of population classes:

- S: Susceptibles, i.e. those individuals who are capable of contracting the disease and might becoming themselves infectives later
- E: Latent individuals, who undergo a latent period, before being themselves capable of transmitting the disease
- I: Infectives, i.e. those individuals who are capable of transmitting the disease to susceptibles
- C: Carriers, i.e. those individuals, who carry and spread the infection disease, but has no clinical symptoms
- R: Removed, i.e. those individuals who have contracted the disease or, if recovered, are permanently immune.

This model can be extended to the $SEICRS$-model with the assumption of possible reinfection even if there were no registered issue for that because it is theoretically possible. From now our aim is to extend and combine the basic $SEICRS$ epidemic model with more influential factors.

The general idea of epidemic spread models is the separation of the whole population into several sub-population having the same properties in some sense. Generally these groups determine the aim structure of epidemic models which are called usually SI, SIR, $SIRS$, $SEIR$, $SEIRS$ or $SEICRS$ model according to the spread direction of the disease. In this paper the last model is developed and investigated because to the best of our knowledge there is no mathematical model describing its mechanism of it. To understand the essence

of this model, it is recommended to analyze simpler models first. When dealing with populations with space structure, the relevant quantities are spatial densities. Firstly we shall define a bounded 2-dimensional domain in $\mathbb{R}^2$ denoted by Ω. Let us denote the number of individuals in group M_i, at a location $x \in \Omega$ and at time $t \geq 0$ by $M_i(x,t)$, where M_i represents one of S, E, I, C or R, i.e $M_i \in \{S, E, I, C, R\}$ for all $i = 1, 2, 3, 4, 5$. It should be noted that x is a 2-dimensional vector in space in domain Ω which coordinates actually representing the geographical degrees of latitude and of longitude. If we denote the number of individuals inside the different groups in the territory Ω for all M_i by

$$M_i^{(\omega)}(t) = \int_{\omega} M_i(z,t)dz\,, \tag{2.1}$$

then the whole population in the habitat ω, denoted by $N^{(\omega)}(t)$ can be specified according to (2.1) as follows:

$$N^{(\omega)}(t) = \sum_{i=1}^{5} M_i^{(\omega)}(t)\,. \tag{2.2}$$

In the further work we assume that habitat ω is a bounded and fixed 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 details, a further operator can be defined 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 [5]. 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 differential equation of the $SEICR$-model system can be formalized as follows with the appropriate initial conditions:

$$
(2.3)\qquad \begin{cases} S'(t) = -\left[\dfrac{\gamma_I(t)}{N(t)} I(t) + \dfrac{\gamma_C(t)}{N(t)} C(t)\right] S(t) + \sigma(t) R(t)\,, \\ E'(t) = \left[\dfrac{\gamma_I(t)}{N(t)} I(t) + \dfrac{\gamma_C(t)}{N(t)} C(t)\right] S(t) - \delta(t) E(t)\,, \\ I'(t) = \delta(t) E(t) - [\varepsilon(t) + \kappa(t)]\, I(t)\,, \\ C'(t) = \varepsilon(t) I(t) - \xi(t) C(t)\,, \\ R'(t) = \xi(t) C(t) - \sigma(t) R(t)\,. \end{cases}
$$

$$
(2.4)\qquad S(0) = S_0,\ \ E(0) = E_0,\ \ I(0) = I_0,\ \ C(0) = C_0,\ \ R(0) = R_0\,.
$$

The flow chart in Figure 1 represents well the one directional connection between groups.

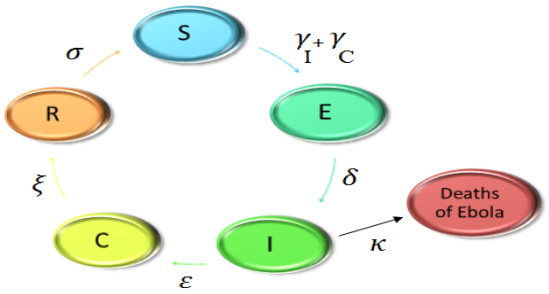

Figure 1. Flow chart about the possible transitions between groups

Here, we have $\gamma_I(t) = p_I(t) \cdot c_I(t)$ and $\gamma_C(t) = p_C(t) \cdot c_C(t)$ 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 $\delta(t)$ denotes the per-capita infectious rate between individuals in latent period and infected humans. In that case, $1/\delta(t)$ becomes the average time for a latent individual to become infectious. $\varepsilon(t)$ marks the rate of individuals who recovered from the virus and are on the mend, but are still infectious. On the other hand $\kappa(t)$ denotes the death rate of the epidemic. Finally $\xi(t)$ stands for the totally recovered humans rate while $\sigma(t)$ 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.

3. Influential factors for the spread of Ebola

3.1. 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 effective 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 $\lambda(t)$ 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 $\kappa_I(t)$ and additionally $\kappa_Q(t)$ mark the death rates of infections caused by the Ebola's epidemic in group I and Q, respectively. Furthermore, let $\varphi(t)$ 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 $\theta(t)$.

With all this in mind we can establish connection between groups after introducing individuals in quarantines and possible vaccination in a flow chart in Figure 2.

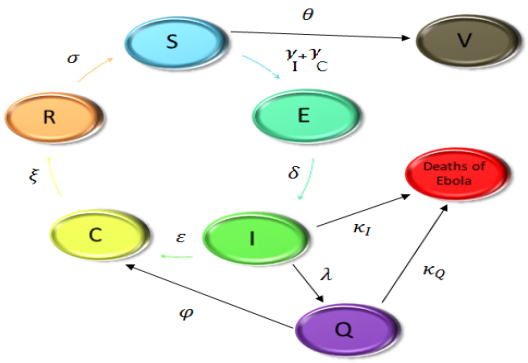

Figure 2. Flow chart of the possible transitions between groups expanded by quarantined and vaccinated individuals.

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 $\theta(t)$ for t, we shall take into consideration the different 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.

3.2. Vital dynamics

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 $\alpha(t)N(t)$ in the susceptible group, where $\alpha(t)$ is a known 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 different in each group and let this rate be denoted in every case by $\beta(t)$ with the appropriate initial letters of various sub-groups in the subscript. We can assume that $\alpha(t)N(t) = \sum_{i=1}^{7} \beta_{M_i}(t)M_i(t)$ for all $t \geq 0$, where M_i denotes the initial identifying the i-th group to be modelled, i.e. $M_i \in \{S, E, I, C, R, Q, V\}$ for $i = 1, 2, 3, 4, 5, 6, 7$. Similarly as before, we establish the connection between the groups in Figure 3 after assuming the vital dynamics.

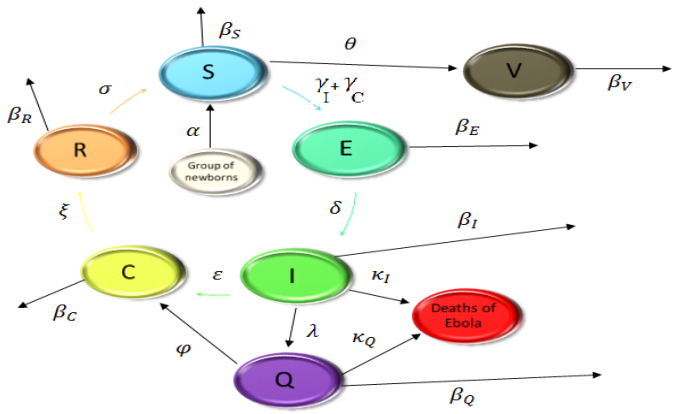

Figure 3. Flow chart of the possible transitions between groups expanded by assuming the vital dynamic.

With these three modifications (i.e. quarantine, vaccination, vital dynamics) we can rewrite the extended form of the system (2.3) with appropriate initial conditions (2.4). Thus we get the following system of ordinary differential equations with initial conditions for the spread of Ebola:

$$
\left\{
\begin{aligned}
S'(t) &= -\left[\frac{\gamma_I(t)}{N(t)}I(t) + \frac{\gamma_C(t)}{N(t)}C(t) + \theta(t) + \beta_S(t)\right] S(t) + \\
&\quad + \sigma(t)R(t) + \alpha(t)N(t)\,, \\
E'(t) &= \left[\frac{\gamma_I(t)}{N(t)}I(t) + \frac{\gamma_C(t)}{N(t)}C(t)\right] S(t) - \left[\delta(t) + \beta_E(t)\right] E(t)\,, \\
I'(t) &= \delta(t)E(t) - \left[\varepsilon(t) + \kappa(t) + \lambda(t) + \beta_I(t)\right] I(t)\,, \\
C'(t) &= \varepsilon(t)I(t) + \varphi(t)Q(t) - \left[\xi(t) + \beta_C(t)\right] C(t)\,, \\
R'(t) &= \xi(t)C(t) - \left[\sigma(t) + \beta_R(t)\right] R(t)\,, \\
Q'(t) &= \lambda(t)I(t) - \left[\kappa_Q(t) + \varphi(t) + \beta_Q(t)\right] Q(t)\,, \\
V'(t) &= \theta(t)S(t) - \beta_V(t)V(t)\,;
\end{aligned}
\right. \tag{3.1}
$$

$$
\left\{
\begin{aligned}
&S(0) = S_0,\ \ E(0) = E_0,\ \ I(0) = I_0,\ \ C(0) = C_0, \\
&\qquad R(0) = R_0,\ \ Q(0) = Q_0,\ \ V(0) = V_0.
\end{aligned}
\right. \tag{3.2}
$$

4. The effect of population migration

The basic importance of space dependent epidemic spread models lies in the distribution of infected individuals inside the population. We suppose that the individuals are continuously on the mend, in consequence reactions (diseases) emerge between different sub-groups. It is important to analyse not isolated populations (no islands or closed biomes). In this work we use only the main results of the proliferation stationary cases of the spatial distributed epidemic spread model developed in [12]. The basic proliferation-stationary system can

be determined for the sub-groups $M_i \in \{S, E, I, C, R, Q, V\}$ for all i as follows

$$\frac{\partial M_i}{\partial t}(x,t) = \int\limits_{\Omega} v(x,y) M_i(y,t) dy - v_e(x) M_i(x,t)\,, \tag{4.1}$$

where domain $\Omega \subset \mathbb{R}^2$ denotes the living space of the population. Additionally the multivalued function $v(x,y)$ is the so called migration rate, and $v_e(x)$ denotes the emigration rate function. Functions $v(x,y)$ and $v_e(x)$ can be defined as follows according to [12]

$$v(x,y) := \lim_{\substack{diam(O_x)\to 0 \\ diam(O_y)\to 0}} \frac{M(O_x,O_y)}{|O_x| M(O_y)}, \;\; v_e(x) := \int\limits_{\Omega} v(y,x) dy\,, \tag{4.2}$$

where $O_x, O_y \in \Omega$ are two disjoint subsets which include x and y points, respectively, furthermore, $M(O_x, O_y)$ represents the number of migrated individuals in a unit time interval from location O_y to O_x, and the whole number of population at place O_y before migration is denoted by $M(O_y)$. Additionally the classical n-dimensional Lebesgue-measure of O_x is denoted by $|O_x|$. We suppose that our migration system has an ergodic property, which means that individuals can migrate from each location to the other place by finite number of steps.

After introducing the classical proliferation-stationary population migration model in (4.1) using notations (4.2), we can transform our extended Ebola epidemic system (3.1) into the form of partial differential equations (PDE), and we can combine it with the proliferation-stationary model in (4.1) according to [12] as follows:

$$\begin{cases} \dfrac{\partial S}{\partial t}(x,t) = -\left[\dfrac{\gamma_I(x,t)}{N(x,t)} I(x,t) + \dfrac{\gamma_C(x,t)}{N(x,t)} C(x,t)\right] S(x,t) + \\ \qquad\qquad - \left[\theta(x,t) + \beta_S(x,t)\right] S(x,t) + \sigma(x,t) R(x,t) + \\ \qquad\qquad + \alpha(x,t) N(x,t) + \displaystyle\int\limits_{\Omega} v(x,y) S(y,t) dy - v_e(x) S(x,t)\,, \\ \dfrac{\partial E}{\partial t}(x,t) = \left[\dfrac{\gamma_I(x,t)}{N(x,t)} I(x,t) + \dfrac{\gamma_C(x,t)}{N(x,t)} C(x,t)\right] S(x,t) - \\ \qquad\qquad - \left[\delta(x,t) + \beta_E(x,t)\right] E(x,t) + \displaystyle\int\limits_{\Omega} v(x,y) E(y,t) dy - \\ \qquad\qquad - v_e(x) E(x,t)\,, \end{cases} \tag{4.3}$$

$$
\begin{cases}
\dfrac{\partial I}{\partial t}(x,t) = \delta(x,t)E(x,t) - \left[\varepsilon(x,t) + \kappa_I(x,t) + \lambda(x,t)\right] I(x,t) + \\
\qquad\qquad -\beta_I(x,t)I(x,t) + \displaystyle\int_\Omega v(x,y)I(y,t)dy - v_e(x)I(x,t)\,, \\
\dfrac{\partial C}{\partial t}(x,t) = \varepsilon(x,t)I(x,t) + \varphi(x,t)Q(x,t) - \xi(x,t)C(x,t) + \\
\qquad\qquad -\beta_C(x,t)C(x,t) + \displaystyle\int_\Omega v(x,y)C(y,t)dy - v_e(x)C(x,t)\,, \\
\dfrac{\partial R}{\partial t}(x,t) = \xi(x,t)C(x,t) - \left[\sigma(x,t) + \beta_R(x,t)\right] R(x,t) + \\
\qquad\qquad + \displaystyle\int_\Omega v(x,y)R(y,t)dy - v_e(x)R(x,t)\,, \\
\dfrac{\partial Q}{\partial t}(x,t) = \lambda(x,t)I(x,t) - \left[\kappa_Q(x,t) + \varphi(x,t) + \beta_Q(x,t)\right] Q(x,t) + \\
\qquad\qquad + \displaystyle\int_\Omega v(x,y)Q(y,t)dy - v_e(x)Q(x,t)\,, \\
\dfrac{\partial V}{\partial t}(x,t) = \theta(x,t)S(x,t) - \beta_V(x,t)V(x,t) \\
\qquad\qquad + \displaystyle\int_\Omega v(x,y)V(y,t)dy - v_e(x)V(x,t)
\end{cases}
\tag{4.3}
$$

with initial conditions

$$
\begin{cases}
S(x,0) = S_0(x), \;\; E(x,0) = E_0(x), \;\; I(x,0) = I_0(x), \\
C(x,0) = C_0(x), \;\; R(x,0) = R_0(x), \;\; Q(x,0) = Q_0(x), \\
V(x,0) = V_0(x).
\end{cases}
\tag{4.4}
$$

Our aim is to apply the sequential splitting algorithm to approximate the solution of the system of PDE's (4.3)-(4.4). For this purpose first we determine the appropriate boundary conditions for points $x \in \partial\Omega$, where $\partial\Omega$ denotes the

boundary of habitat Ω. To do that we use the classical Neumann-boundary conditions which defines the flux (combination of immigration and emigration rate) of individuals at $\partial\Omega$. We suppose that this flux depends on time and on the location uniformly. In mathematical formulation this means the following

$$\frac{\partial M_i}{\partial x}(\tilde{x},t) = \Psi_{M_i}(\tilde{x},t), \;\; \tilde{x} \in \partial\Omega, \;\; t \in [0,T]\,. \tag{4.5}$$

The last thing we need to do is determining functions $\Psi_{M_i}(\tilde{x},t)$ for every sub-group, namely, for all $M_i \in \{S,E,I,C,R,Q,V\}$.

We 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 flux at the boundary is much lower. The flux 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.

If we accept these assumptions, we can actually define arbitrarily functions $\Psi_{M_i}(\tilde{x},t)$ for all M_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

$$\Psi_{M_i}(\tilde{x},t) := \frac{\tilde{k_i}(\tilde{x})}{\sqrt{2\pi}} e^{-\frac{(t-m_i)}{2}}, \;\; \tilde{x} \in \partial\Omega, \;\; t \in [0,T]\,, \tag{4.6}$$

where $\tilde{k_i}(\tilde{x})$ denotes the flux constant for all locations at the boundary of the domain for the different sub-groups (S,E,I,C,R,Q,V).

In the next section we describe the basics of sequential splitting solution and we determine an algorithm to find the approximated solution of the Ebola epidemic spread model (4.3) with the given initial (4.4) and boundary conditions (4.5)-(4.6).

5. Sequential splitting and the numerical scheme

Splitting methods are generally used to solve partial differential equations or system of equations [8], [9], [10]. The main idea is to replace the complex problem with the sequence of sub-problems with simpler structure. In the following the general method of sequential splitting [11] 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 $x \in [0,L]$

$$\text{(5.1)} \qquad \begin{cases} \dfrac{\partial w(x,t)}{\partial t} = \displaystyle\sum_{i=1}^{n} A_i w(x,t) \\ \\ w(x,0) = w_0(x), \;\; \dfrac{\partial w(0,t)}{\partial x} = g_1(t), \;\; \dfrac{\partial w(L,t)}{\partial x} = g_2(t) \end{cases}$$

where $w : \mathbb{R} \times \mathbb{R} \to \Lambda$ is the Λ-valued unknown function for every fixed $t \in [0,T]$ and Λ denotes the possible states space, which is usually assumed to be a Banach space. Furthermore $w_0(x) \in \Lambda$ and $g_1(t)$, $g_2(t) \in \Lambda$ define the initial and boundary conditions of the problem, and operators $A_i : \Lambda \to \Lambda$ define the different sub-processes. Operator splitting techniques were developed to find the solution of problem (5.1), when A_i consists of non-linear operator(s). Usually operators are split 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 (5.1) 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 the macroscopic problem. Let $\omega_{h,\tau}^{mac}$ be a mesh, which consists of (x_i, t_k) mesh-points, where h and τ denote the chosen spatial and time resolution of the mesh, according to the following

$$\text{(5.2)} \qquad \begin{aligned} x_i &= ih, \;\; h = \tfrac{L}{N_L} \;\; i = 0,1,2,\ldots,N_L \\ t_k &= k\tau, \;\; \tau = \tfrac{T}{N_T} \;\; k = 0,1,2,\ldots,N_T \end{aligned}$$

where N_L and N_T denote the numbers of division parts in space and time. Then we introduce a finer mesh for the microscopic problem. Let this mesh be denoted by $\omega_{h,\Delta\tau}^{mic}$ which consists of the (x_i, t_n) mesh-points, where h and $\Delta\tau$ denote the chosen spatial and time resolution, respectively. In this case

$$
\begin{aligned}
&x_i = ih, \;\; h = \tfrac{L}{N_L} \;\; i = 0, 1, 2, \ldots, N_L \\
&t_n = n\Delta\tau, \;\; \Delta\tau = \tfrac{\tau}{N_\tau} \;\; n = 0, 1, 2, \ldots, N_T \cdot N_\tau
\end{aligned}
\tag{5.3}
$$

where N_τ marks the number of subdivision parts in time and space. Note that perceive that $N_T \cdot N_\tau \cdot \Delta\tau = N_T \cdot \tau = T$ which means that the time interval is the same as by mesh $\omega_{h,\tau}^{mac}$, only with finer time steps.

There are two things worth mentioning: First, $\omega_{h,\tau}^{mic}$ contains every point from mesh $\omega_{h,\tau}^{mac}$ and additionally extra points. Alternatively the two mesh-points are not necessarily required to overlap, but this case is not investigated here. Second, the spatial resolution of the mesh is not changed, because the convergence criterion for FDM is linked with time through $\frac{\Delta\tau}{h^2}$. Hereinafter the introduction of a corresponding vector space $\Xi(\omega_{h,\Delta\tau}^{mic})$ is needed, where the approximated mesh-functions are interpreted on $\omega_{h,\Delta\tau}^{mic}$ (defined in (5.3)). Our aim is to find series of mesh-functions $(y_i^n)_j := (y_{h,\Delta\tau})_j (x_i, t_n) \in \Xi(\omega_{h,\Delta\tau}^{mic})$ which approximates well the j-th components of vector function $(\vec{w})_j (x_i, t_n)$ at the mesh-point $(x_i, t_n) \in \omega_{h,\Delta\tau}^{mic}$. Let us denote by $j = 1, 2, 3, 4, 5, 6, 7$ the components of the solution S, E, I, C, R, Q and V, respectively.

First and last, the original problem (or the operator of the problem) is split into macroscopic (Problem 1) and microscopic (Problem 2) sub-problems. The sequential splitting method solves the sub-problem iteratively by applying the steps depicted in Figure 4.

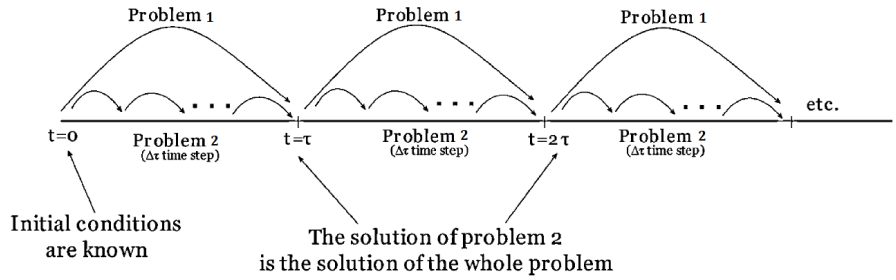

Figure 4. The flow chart of sequential splitting algorithm on macroscopic (Problem 1) and microscopic (Problem 2) sub-problems [10].

The following algorithm describes the solution sequence of the sub-problems where $t \in [0, T]$ and $x \in [0, L]$ on the above defined meshes. In the first step of the algorithm, both sub-problems are considered on the interval $[0, \tau]$.

Problem 1 - Normal mesh (macroscopic)

$$
\begin{cases}
\dfrac{\partial \left(\vec{w}_1^{(1)}\right)_j}{\partial t}(x,t) = \displaystyle\sum_{i=1}^{k} A_i \left(\vec{w}_1^{(1)}\right)_j (x,t) \\
\left(\vec{w}_1^{(1)}\right)_j (x,0) = \left(\vec{w}_0\right)_j (x) \\
\dfrac{\partial \left(\vec{w}_1^{(1)}\right)_j}{\partial x}(0,t) = (g_1)_j (t), \quad \dfrac{\partial \left(\vec{w}_1^{(1)}\right)_j}{\partial x}(L,t) = (g_2)_j (t)
\end{cases} \tag{5.4}
$$

Problem 2 - Finer mesh (microscopic)

$$
\begin{cases}
\dfrac{\partial \left(\vec{w}_2^{(1)}\right)_j}{\partial t}(x,t) = \displaystyle\sum_{i=k+1}^{n} A_i \left(\vec{w}_2^{(1)}\right)_j (x,t) \\
\left(\vec{w}_2^{(1)}\right)_j (x,0) = \left(\vec{w}_1^{(1)}\right)_j (x,\tau) \\
\dfrac{\partial \left(\vec{w}_2^{(1)}\right)_j}{\partial x}(0,t) = (g_1)_j (t), \quad \dfrac{\partial \left(\vec{w}_2^{(1)}\right)_j}{\partial x}(L,t) = (g_2)_j (t)
\end{cases} \tag{5.5}
$$

The subscript of $\vec{w}$ corresponds to the solution of each sub-problem and the superscript is the splitting step. Furthermore Problem 2 is solved independently N_τ times to reach the solution at point τ, because $N_\tau \cdot \Delta\tau = \tau$.

In the second step we solve the PDE applying the operator in Problem 1 iteratively but now on time interval $[\tau, 2\tau]$ time interval with initial condition $w_2^{(1)}(x,\tau)$ and so forth in the following steps of the algorithm. By solving the previous n steps iteratively, the constructed $w_2^{(n)}(x,n\tau)$ is the solution of the sequential splitting on the given $\Xi(\omega_{h,\Delta\tau}^{mic})$ mesh.

The splitted solution of the PDE-system is approximated in this work by explicit Euler scheme which consists of explicit approaches on both sub-problems.

6. Qualitative properties of a simplified model

The model (4.3) is too complex to analyze or determine any qualitative properties of it. Hence, in this section we simplify (4.3) into a system of partial-

integro-differential equations (PIDE) with one variable. Our aim is now to say something about the connection of the continuous and the discretized model for the general form of PIDEs.

Starting with the reduction of (4.3) with initial (4.4) and boundary conditions (4.5)–(4.6) we define the following PIDE

$$\text{(6.1)}\qquad \begin{cases} \dfrac{\partial \eta}{\partial t}(x,t) = F(x,t,\eta(x,t)) + G(\eta(x,t)), \;\; x \in [0,1], \;\; t \in [0,T]\,, \\ \eta(x,0) = \eta_0(x), \;\; x \in [0,1]\,, \\ \dfrac{\partial \eta}{\partial x}(x,t) = \dfrac{k}{\sqrt{2\pi}} e^{-\frac{(t-m)}{2}}, \;\; x \in \{0,1\}, \;\; t \in [0,T]\,, \end{cases}$$

where F is a nonlinear positive function and G is the classical definite integral operator, namely

$$\text{(6.2)}\qquad G(\eta(x,t)) := \int_0^1 \eta(x,t)dx.$$

The discretized form of (6.1) can be determined applying the explicit Euler scheme on F and the trapezoidal rule on G and considering the mesh $\omega^{mic}_{h,\Delta\tau}$ in (5.3) as follows for all $i = 1,2,\ldots,N_L$ and $n = 1,2,\ldots,N_T \cdot N_\tau$:

$$\text{(6.3)}\qquad \begin{cases} \dfrac{\eta_i^n - \eta_i^{n-1}}{\Delta\tau} = F_i^{n-1} + \dfrac{h}{2}\left(\eta_i^{n-1} - \eta_{i-1}^{n-1}\right)\,, \\ \eta_i^0 = \eta_0(x_i)\,, \\ \dfrac{\eta_1^n - \eta_0^n}{h} = \dfrac{k}{\sqrt{2\pi}} e^{-\frac{(t_n-m)}{2}}, \;\; \dfrac{\eta_{N_L}^n - \eta_{N_L-1}^n}{h} = \dfrac{k}{\sqrt{2\pi}} e^{-\frac{(t_n-m)}{2}}\,. \end{cases}$$

It is an essential expectation from the discretized model (6.3) to have the equivalent qualitative properties with the continuous model (6.1). From this purpose we investigate if the discretized model preserve the non-negativity and give some further condition which guarantees this property. Keeping non-negativity means that the initial condition $\eta_i^0 \geq 0$ for any $i = 1,2,\ldots,N_L$ implies that $\eta_i^n \geq 0$ for all $i = 0,1,\ldots,N_L$ and $n = 0,1,\ldots,N_T \cdot N_\tau$.

Let us consider according to the sequential splitting algorithm as discretized macroscopic and microscopic problems the following equations in every algorithm step and for all i and n. As a microscopic problem we shall consider the equation

$$\text{(6.4)}\qquad \frac{\eta_{1,i}^n - \eta_{1,i}^{n-1}}{\Delta\tau} = F_i^{n-1}$$

and in the same manner as a macroscopic problem the equation

$$\frac{\eta_{2,i}^{n}-\eta_{2,i}^{n-1}}{\tau}=\frac{h}{2}\left(\eta_{2,i}^{n-1}-\eta_{2,i-1}^{n-1}\right), \tag{6.5}$$

where the subscripts denote the number of sub-problems.

From Section 5 we know that (6.4) and (6.5) are connected to each other by the appropriate initial conditions. Hence, we need to analyze the non-negativity of (6.4) and (6.5) simultaneously.

$\eta_{1,i}^{n}$ in (6.4) is trivially non-negative because F was defined as a positive multivalued function. Taking this and $\eta_{1,i}^{0}\geq 0$ into consideration one can easily check that $\eta_{1,i}^{n}\geq 0$ for all n and i. However the value of $\eta_{2,i}^{n}$ depends on the solution of (6.4), therefore we use and proof the following statement.

Statement 6.1. *Let us suppose that for the initial condition in* (6.5) *the inequality* $\eta_{2,i}^{0}\geq 0$ *holds for all* $i=0,1,\ldots,N_L$ *and for the discrete values of function* F*, namely for* F_i^1*,* F_j^1 *the following inequalities hold:*

$$\left(1+\frac{2}{\tau h}\right)\eta_{2,i}^{0}\geq\eta_{2,j}^{0} \text{ and } \left(1+\frac{2}{\tau h}\right)F_i^1\geq F_j^1 \text{ for all } i\neq j. \tag{6.6}$$

Then for all $n=1,2,\ldots,N_T\cdot N_\tau$ *and* $i=0,1,\ldots,N_L$ *the discrete value of* $\eta_{2,i}^{n}$ *holds the non-negativity.*

Proof. We prove our statement with induction. Hence $\eta_{2,i}^{0}\geq 0$ for all $i=0,1,\ldots,N_L$ according to (6.5) one can see that

$$\eta_{2,i}^{1}=\left(1+\frac{\tau h}{2}\right)\eta_{2,i}^{0}-\frac{\tau h}{2}\eta_{2,i-1}^{0}.$$

Since $\eta_{2,i}^{0}$ and $\eta_{2,j}^{0}$ hold the inequality (6.6), we can obtain that

$$\left(1+\frac{2}{\tau h}\right)\eta_{2,i}^{0}\geq\eta_{2,j}^{0} \text{ for all } i\neq j.$$

holds. Therefore, for $n=0$ the non-negativity is clear.

Let $k-1$ be a fixed index and suppose that Statement 6.1 holds for $\eta_{2,i}^{k-1}$ for all $i=0,1,\ldots,N_L$. Now we prove that $\eta_{2,i}^{k}\geq 0$ holds uniformly on the same manner such as in case of $\eta_{2,i}^{0}$. Finally we need to show, that inequalities, defined in (6.6), imply the followings

$$\left(1+\frac{2}{\tau h}\right)\eta_{2,i}^{n}\geq\eta_{2,j}^{n} \text{ and } \left(1+\frac{2}{\tau h}\right)F_i^{n+1}\geq F_j^{n+1} \tag{6.7}$$

for all $i \neq j$ for fixed $n = 1, 2, \ldots, N_T \cdot N_\tau$.

We assume now that (6.7) holds for a fixed $n-1$. Using this we prove by mathematical induction that (6.7) holds for n. Since (6.4) and (6.5) are connected through their initial conditions, we can see that for fixed n the equality

$$\eta_{1,i}^n = \eta_{2,i}^{n-1} \text{ for all } i \neq j$$

holds. Therefore, (6.4) implies that

$$\eta_{1,i}^n = \eta_{2,i}^{n-1} = \Delta\tau F_i^{n-1} + \eta_{2,i}^{n-2}$$

which yields after re-arrangement and substitution into (6.7) the inequality

$$\left(1 + \frac{2}{\tau h}\right) \Delta\tau F_i^n + \left(1 + \frac{2}{\tau h}\right) \eta_{2,i}^{n-1} \geq \Delta\tau F_{i-1}^n + \eta_{2,i-1}^{n-1} \tag{6.8}$$

Hence

$$F_i^n = \frac{\eta_{2,i}^n - \eta_{2,i}^{n-1}}{\Delta\tau} \text{ and } F_{i-1}^n = \frac{\eta_{2,i-1}^n - \eta_{2,i-1}^{n-1}}{\Delta\tau}$$

holds uniformly and using our induction assumption for $\eta_{2,i}^{n-1}$ and F_i^n after substitution to (6.8) we get the following inequality

$$\begin{aligned} \left(1 + \frac{2}{\tau h}\right) \eta_{2,i}^n - \left(1 + \frac{2}{\tau h}\right) \eta_{2,i}^{n-1} \geq \eta_{2,i-1}^n - \eta_{2,i-1}^{n-1} \geq \\ \geq \eta_{2,i-1}^n - \left(1 + \frac{2}{\tau h}\right) \eta_{2,i}^{n-1}, \end{aligned} \tag{6.9}$$

which yields the inequality (6.7) for a fixed index n. Using (6.9) it can be shown in the same way that (6.7) holds for F_i^{n+1}. ■

7. Numerical testing

In the last section we turn back to the numerical testing of the developed PIDE-system defined in (4.3) with appropriate initial (4.4) and boundary conditions (4.5)-(4.6). As numerical solution algorithm we use the sub-problems of sequential splitting defined in (5.4)-(5.5). We take the integral-part (migration factor) as the macroscopic and the differential part (epidemic spread) as the microscopic problem. For simplicity in this work we analyze only the one-dimensional system on the space interval $[0, L]$ and time interval $[0, T]$. Furthermore all time and space dependent parameter functions are supposed

to be used as constant functions. In favour of better visibility we normalized the initial parameters according to the whole population.

We apply the explicit Euler numerical scheme on the system and we implement the split solution solved by sequential splitting. The examined time and space intervals are chosen as $[0, 5]$ and $[0, 1]$. Let us consider a mesh with micro time step size $\Delta\tau$, macro time step size τ and spatial step size h chosen as 0.01, 0.1 and 0.01, respectively. With all this in mind we implement the results in Figure 5.

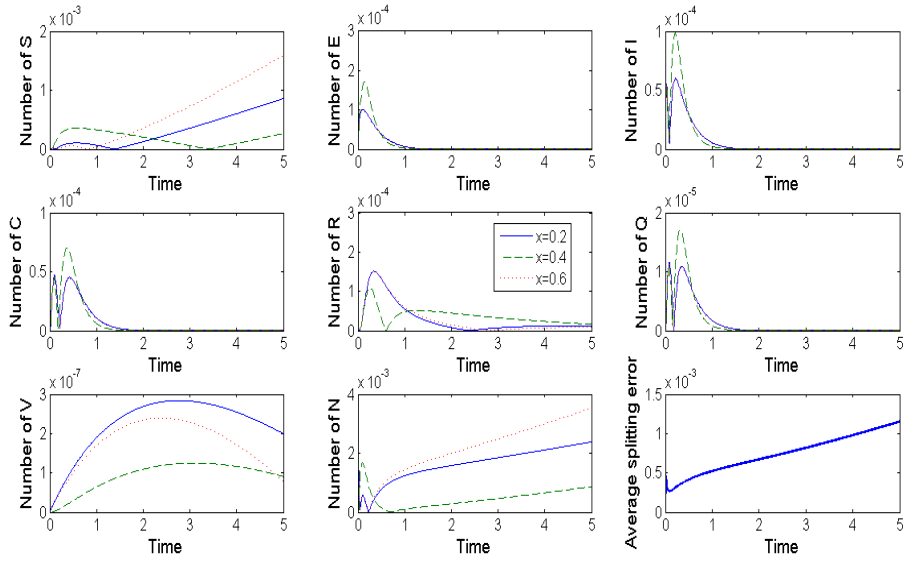

Figure 5. Solution functions of various groups and total population. Last figure implement the average error of sequential splitting in space and time.

Blue continuous, red dotted and green dashed lines represent actually the motion at three different location. Subplots in Figure 5 represent the behaviour of individuals in the sub-group of suspectibles, latents, infected, carriers, removed, quarantined and vaccinated, respectively, since the last sub-plot implement the absolute error of sequential splitting, averaged in space, compared with the reference solution calculated without splitting by using the explicit Euler method on a very fine time and space mesh.

The middle-bottom part of Figure 5 shows that the number of the whole population decreases at the beginning of the 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 in a faster manner. It can be concluded that the population will not be 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 a respectably small number of infected individuals.

The top-middle part of Figure 3 shows the numerical behaviour of the subpopulations after infection. The function of the infected individuals shows a strongly decreasing behaviour because of the very small reinfection-rate (σ) and the really big mortality rate (κ). The compartments of individuals immediately before (E), after infection (C) 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, and so does the number number of infected people. The size of the group of recovered and vaccinated individuals 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 individual survived the virus. Obviously the increasing speed is high only at the beginning of the epidemic.

The analysis of error figures on the right-bottom part of Figure 5 indicates the conclusion that the system is not sensitive to the splitting algorithm, the error's order is approximately 10^{-3}.

8. Conclusion and further work

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-differential equations (PIDEs) by using time and space dependency. We have developed the simplified form of the general PIDEs in continuous and in discretized form, as well. We concluded that the space and time discretized model has the non-negativity preservation such as the continuous model under some rational conditions.

Furthermore we determined that the sequential splitting algorithm based on the explicit Euler scheme is effective to approximate the solution numerically. The main conclusion is that the operator splitting technique can be applied easily to extend the existing model by other influential 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 affect the spread of the virus. As further numerical analysis, the convergence of the numerical model, investigation of the properties and solutions of different operator splitting techniques or numerical schemes can be interesting, as well.

Finally, we mention that the accurate modelling of disease spread of Ebola is essential to give some preventative suggestions to predict the virus and rescue thousands of people.

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