Multiregional SIR Model with Infection during Transportation

Diána H. Knipl[*] and Gergely Röst[†]

[*]Analysis and Stochastics Research Group – Hungarian Academy of Sciences,
Bolyai Institute, University of Szeged, Szeged, Hungary
Email: knipl@math.u-szeged.hu
[†] Bolyai Institute, University of Szeged, Szeged, Hungary
Email: rost@math.u-szeged.hu

Abstract—We present a general epidemic model to describe the spread of an infectious disease in several regions connected by transportation. We take into account that infected individuals not only carry the disease to a new place while traveling from one region to another, but transmit the disease during travel as well. We obtain that a model structured by travel time is equivalent to a large system of differential equations with multiple delays. By showing the local Lipschitz property of the dynamically defined delayed feedback function, we obtain existence and uniqueness of solutions of the system.

Keywords-epidemic spread; transportation model; dynamically defined delay; Lipschitz continuity

I. INTRODUCTION

We consider an arbitrary n number of regions which are connected by transportation, and present an SIR based model which describes the spread of infection in the regions and also during travel between them. We show that our model is equivalent to a system of functional differential equations

$$x'(t) = \mathcal{F}(x_t), \qquad (1)$$

where $t \in \mathbb{R}$, $t \geq 0$ and $x : \mathbb{R} \to \mathbb{R}^{3n}$. We use the notation $x_t \in \mathcal{C}$, $x_t(\theta) = x(t + \theta)$ for $\theta \in [-\sigma, 0]$, where for $\sigma > 0$, we define our phase space $\mathcal{C} = \mathcal{C}([-\sigma, 0], \mathbb{R}^{3n})$ as the Banach space of continuous functions from $[-\sigma, 0]$ to $\mathbb{R}^{3n}$, equipped with the usual supremum norm $|| \cdot ||$. In the sequel we use the notation $|v|$ for the Euclidean

TABLE I
VARIABLES AND KEY MODEL PARAMETERS ($j, k \in \{1, \ldots n\}$)

S_j, I_j, R_j, N_j	susceptible, infected, recovered, all individuals in region j
$s_{k,j}$, $i_{k,j}$, $r_{k,j}$, $n_{k,j}$	susceptible, infected, recovered, all individuals during travel from region k to j
Λ_j	incidence in region j
$\lambda_{k,j}$	incidence during travel from region k to j
α_j	recovery rate of infected individuals in region j
$\alpha_{k,j}$	recovery rate during travel from region k to j
$\mu_{j,k}$	travel rate from region j to region k
$\tau_{k,j}$	duration of travel from region k to j

norm of any vector $v \in \mathbb{R}^m$ for $m \in \mathbb{Z}_+$. In order to obtain the general existence and uniqueness result for the system, we prove that $\mathcal{F} : \mathcal{C} \to \mathbb{R}^{3n}$ satisfies the local Lipschitz condition on each bounded subset of $\mathcal{C}$, that is, for every $M > 0$ there exists a constant $K = K(M)$ such that the inequality $|\mathcal{F}(\phi) - \mathcal{F}(\psi)| \leq K||\phi - \psi||$ holds for every $\phi, \psi \in \mathcal{C}$ with $||\phi||, ||\psi|| \leq M$.

The paper is organised as follows. In Section 2 we introduce our model, then we obtain the compact form of the system in Section 3. Section 4 concerns with the proof of the local Lipschitz condition for various types of incidence (new cases per unit of time).

II. MODEL DESCRIPTION

We formulate a dynamical model describing the spread of an infectious disease in n regions and also during travel from one region to another. Divide the entire populations of the n regions into the disjoint classes S_j, I_j, R_j, $j \in \{1, \ldots n\}$, where $S_j(t)$ $I_j(t)$, $R_j(t)$, $j \in \{1, \ldots n\}$ denote the number of susceptible, infected and recovered individuals at time t in region j. For the total population in region j at time t, we use the notation

$$N_j(t) = S_j(t) + I_j(t) + R_j(t).$$

The incidence in region j is denoted by $\Lambda_j\big(S_j(t), I_j(t), R_j(t)\big)$, model parameter α_j represents the recovery rate of infected individuals in region j. We denote the travel rate from region j to region k by $\mu_{j,k}$ and we set $\mu_{j,j} = 0$ for $j, k \in \{1, \ldots n\}$.

Let $s_{k,j}$, $i_{k,j}$, $r_{k,j}$ denote susceptible, infected and recovered travelers, where lower index-pair $\{k,j\}$, $j, k \in \{1, \ldots n\}$ indicates that individuals are traveling from region k to region j. Let $\tau_{k,j} > 0$ denote the time required to complete the travel from region k to region j, which is assumed to be fixed. To describe the disease dynamics during travel, for each t_* we define $s_{k,j}(u; t_*)$, $i_{k,j}(u; t_*)$, $r_{k,j}(u; t_*)$, $j, k \in \{1, \ldots n\}$ as the densities of individuals with respect to u who started travel at time t_* and belong to classes $s_{k,j}$, $i_{k,j}$, $r_{k,j}$, where $u \in [0, \tau_{k,j}]$ denotes the time elapsed since the beginning of the travel. Then $s_{k,j}(\tau_{k,j}; t - \tau_{k,j})$, $i_{k,j}(\tau_{k,j}; t - \tau_{k,j})$, $r_{k,j}(\tau_{k,j}; t - \tau_{k,j})$ express the inflow of individuals arriving from region k to compartments S_j, I_j, R_j at time t, respectively. Let

$$n_{k,j}(u; t_*) = s_{k,j}(u; t_*) + i_{k,j}(u; t_*) + r_{k,j}(u; t_*)$$

denote the total density of individuals during travel from region k to j, where $j, k \in \{1, \ldots n\}$. The total density is constant during travel, i.e. $n_{k,j}(u; t_*) = n_{k,j}(0, t_*)$ for all $u \in [0, \tau_{k,j}]$. During the course of travel from region k to j, $\lambda_{k,j}\big(s_{k,j}(u; t_*), i_{k,j}(u; t_*), r_{k,j}(u; t_*)\big)$ represents the incidence, and let $\alpha_{k,j}$ denote the recovery rate. All variables and model parameters are listed in Table I. Based on the assumptions formulated above, we obtain the following system of differential equations for the

disease transmission in region j, $j \in \{1, \ldots n\}$:

$$
\begin{cases}
\dot{S}_j(t) = -\Lambda_j(\cdot) - \left(\sum_{k=1}^n \mu_{j,k}\right) S_j(t) \\
\qquad + \sum_{k=1}^n s_{k,j}(\tau_{k,j}; t - \tau_{k,j}), \\
\dot{I}_j(t) = \Lambda_j(\cdot) - \left(\sum_{k=1}^n \mu_{j,k}\right) I_j(t) \\
\qquad - \alpha_j I_j(t) + \sum_{k=1}^n i_{k,j}(\tau_{k,j}; t - \tau_{k,j}), \\
\dot{R}_j(t) = \alpha_j I_j(t) - \left(\sum_{k=1}^n \mu_{j,k}\right) R_j(t) \\
\qquad + \sum_{k=1}^n r_{k,j}(\tau_{k,j}; t - \tau_{k,j}).
\end{cases}
\quad (L_j)
$$

For each $j, k \in \{1, \ldots n\}$ and for each t_*, the following system $(T_{k,j})$ describes the evolution of the densities during the travel from region k to region j which started at time t_*:

$$
\begin{cases}
\dfrac{d}{du} s_{k,j}(u; t_*) = -\lambda_{k,j}(\cdot), \\
\dfrac{d}{du} i_{k,j}(u; t_*) = \lambda_{k,j}(\cdot) - \alpha_{k,j} i_{k,j}(u; t_*), \\
\dfrac{d}{du} r_{k,j}(u; t_*) = \alpha_{k,j} i_{k,j}(u; t_*).
\end{cases}
\quad (T_{k,j})
$$

For sake of simplicity, in systems (L_j) and $(T_{k,j})$ we use the notations $\Lambda_j(\cdot)$ and $\lambda_{k,j}(\cdot)$ for the incidences, where these functions are meant to be evaluated at the appropriate points. For $u = 0$, the densities are determined by the rates individuals start their travels from region k to region j at time t_*. Hence, the initial values for system $(T_{k,j})$ at $u = 0$ are given by

$$
\begin{cases}
s_{k,j}(0; t_*) = \mu_{k,j} S_k(t_*), \\
i_{k,j}(0; t_*) = \mu_{k,j} I_k(t_*), \\
r_{k,j}(0; t_*) = \mu_{k,j} R_k(t_*).
\end{cases}
\quad (IVT_{k,j})
$$

Notice that $\mu_{j,j} = 0$ for $j \in \{1, \ldots n\}$ implies that for each t_*, it holds that $s_{j,j}(u; t_*) = i_{j,j}(u; t_*) = r_{j,j}(u; t_*) \equiv 0$, as there is no travel from region j to itself. Since travel from region k to region j takes $\tau_{k,j}$ units of time to complete, we need to assure that there exists a unique solution of system $(T_{k,j})$ on $[0, \tau_{k,j}]$ (see Proposition IV.1).

Now we turn our attention to the terms $s_{k,j}(\tau_{k,j}; t - \tau_{k,j})$, $i_{k,j}(\tau_{k,j}; t - \tau_{k,j})$, $r_{k,j}(\tau_{k,j}; t - \tau_{k,j})$, $j, k \in \{1, \ldots n\}$ in

system (L_j), which give the inflow of individuals arriving to classes S_j, I_j, R_j at time t, upon completing a travel from region k. At time t, these terms are determined by the solution of system $(T_{k,j})$ at $u = \tau_{k,j}$ with initial values $(IVT_{k,j})$ for $t_* = t - \tau_{k,j}$, since individuals who left region k with rate $\mu_{k,j}$ at time $t - \tau_{k,j}$ will enter region j at time t.

Next we specify initial values for system (L_j) at $t = 0$. Since for $k \in \{1, \dots n\}$, travel from region k to region j takes $\tau_{k,j}$ units of time to complete, arrivals to region j at time t are determined by the state of the classes of region k at $t - \tau_{k,j}$, via the solution of system $(T_{k,j})$ and initial values $(IVT_{k,j})$. Thus, we set up initial values as follows:

$$\begin{cases} S_j(\theta) = \varphi_{S,j}(\theta), \\ I_j(\theta) = \varphi_{I,j}(\theta), & (IVL_j) \\ R_j(\theta) = \varphi_{R,j}(\theta), \end{cases}$$

where $\theta \in [-\tau, 0]$ for $\tau := \max_{j,k \in \{1,\dots n\}} \tau_{k,j}$, moreover $\varphi_{S,j}$, $\varphi_{I,j}$ and $\varphi_{R,j}$ are continuous functions for $j \in \{1, \dots n\}$.

III. THE COMPACT FORM OF THE SYSTEM

For each $j, k \in \{1, \dots n\}$ and $t_* \geq 0$, we define $y(u) = y_{k,j}^{t_*}(u) = (s_{k,j}(u; t_*), i_{k,j}(u; t_*), r_{k,j}(u; t_*))^T$ and $g = g_{k,j} = (g_S, g_I, g_R)^T$, where $y : [0, \tau_{k,j}] \to \mathbb{R}^3$, $g : \mathbb{R}^3 \to \mathbb{R}^3$ and

$$g_S(y) = -\lambda_{k,j}(y_1, y_2, y_3),$$
$$g_I(y) = \lambda_{k,j}(y_1, y_2, y_3) - \alpha_{k,j} y_2,$$
$$g_R(y) = \alpha_{k,j} y_2.$$

Then for each j, k and t_*, system

$$\begin{cases} y'(u) = g(y(u)), \\ y(0) = y_0 \end{cases} \quad (2)$$

is a compact form of system $(T_{k,j})$ with initial values $(IVT_{k,j})$ for $y_0 = (\mu_{k,j} S_k(t_*), \mu_{k,j} I_k(t_*), \mu_{k,j} R_k(t_*))^T$. Let $y(u, 0; y_0)$ denote the solution of system (2) at time u with initial value y_0.

The feasible phase space is the nonnegative cone $\mathcal{C}_+ = \mathcal{C}([-\tau, 0], \mathbb{R}_+^{3n})$ of the Banach space of continuous functions from $[-\tau, 0]$ to $\mathbb{R}^{3n}$ with the sup norm. For every $j, k \in \{1, \dots n\}$, let $h_{k,j} : \mathbb{R}^{3n} \to \mathbb{R}^3$ be defined by $h_{k,j} = (h_{S,k,j}, h_{I,k,j}, h_{R,k,j})^T$, where

$$h_{S,k,j}(v) = \mu_{k,j} v_{3k-2},$$
$$h_{I,k,j}(v) = \mu_{k,j} v_{3k-1},$$
$$h_{R,k,j}(v) = \mu_{k,j} v_{3k}.$$

For $\phi \in \mathcal{C}_+$, we use the notation $\hat{y}_{\phi(-\tau_{k,j})}(u) = y(u, 0; h_{k,j}(\phi(-\tau_{k,j})))$. Furthermore we define $W_k : \mathcal{C}_+ \to \mathbb{R}^{3n}$ as

$$W_k(\phi) = \left(\hat{y}_{\phi(-\tau_{k,1})}(\tau_{k,1}), \dots \hat{y}_{\phi(-\tau_{k,n})}(\tau_{k,n})\right)^T.$$

Let $x(t) = (S_1(t), I_1(t), R_1(t), \dots S_n(t), I_n(t), R_n(t))^T$ for $t \geq 0$, and $f = (f_{S,1}, f_{I,1}, f_{R,1}, \dots f_{S,n}, f_{I,n}, f_{R,n})^T$, where for $j \in \{1, \dots n\}$,

$$f_{S,j}(x) = -\Lambda_j(x_{3j-2}, x_{3j-1}, x_{3j}) - \left(\sum_{k=1}^n \mu_{j,k}\right) x_{3j-2},$$

$$f_{I,j}(x) = \Lambda_j(x_{3j-2}, x_{3j-1}, x_{3j}) - \alpha_j x_{3j-1}$$
$$- \left(\sum_{k=1}^n \mu_{j,k}\right) x_{3j-1},$$

$$f_{R,j}(x) = \alpha_j x_{3j-1} - \left(\sum_{k=1}^n \mu_{j,k}\right) x_{3j}.$$

Clearly the union of systems (L_j) with initial conditions (IVL_j), $j \in \{1, \dots n\}$ can be written in a closed form as

$$\begin{cases} x'(t) = f(x(t)) + \sum_{k=1}^n W_k(x_t) =: \mathcal{F}(x_t), \\ x_0 = \varphi, \end{cases} \quad (3)$$

where $\mathcal{F} : \mathcal{C}_+ \to \mathbb{R}^{3n}$ and for $\varphi \in \mathcal{C}_+$, $\varphi := (\varphi_{S,1}, \varphi_{I,1}, \varphi_{R,1}, \dots, \varphi_{S,n}, \varphi_{I,n}, \varphi_{R,n})^T$.

IV. THE LOCAL LIPSCHITZ PROPERTY

This section is devoted to the proof of the general existence and uniqueness result of system (3). First, we obtain the following simple result.

Proposition IV.1. *Assume that $\lambda_{k,j}$ possesses the local Lipschitz property on each bounded subset of $\mathbb{R}^3$. Moreover, assume that $\lambda_{k,j}(q_1, q_2, q_3) \geq 0$ and $\lambda_{k,j}(0, q_2, q_3) = 0$ hold for $q_1, q_2, q_3 \geq 0$. Then there exists a unique solution of system (2) which continuously depends on the initial data, and for $u \in [0, \tau]$ and $y_0 \geq 0$ the following inequality holds componentwise:*

$$0 \leq y(u, 0; y_0) \leq \sqrt{3} |y_0|.$$

Proof: The local Lipschitz condition guarantees the existence of a unique solution which continuously depends on the initial data (see Picard-Lindelöf theorem in Chapter II, Theorem 1.1 and Chapter V, Theorem 2.1 in [1]). We have also seen that $n_{k,j}(u; t_*)$ is constant for all u in the maximal interval of existence, moreover from the nonnegativity condition of $\lambda_{k,j}$ it follows that

nonnegative initial data give rise to nonnegative solution. Hence we obtain

$$
\begin{aligned}
0 &\le n_{k,j}(0;t_*) = n_{k,j}(u;t_*), \\
0 &\le s_{k,j}(0;t_*) + i_{k,j}(0;t_*) + r_{k,j}(0;t_*) \\
&= s_{k,j}(u;t_*) + i_{k,j}(u;t_*) + r_{k,j}(u;t_*) \\
&= \mu_{k,j}(S_k(t_*) + I_k(t_*) + R_k(t_*)), \\
0 &\le s_{k,j}(u;t_*), i_{k,j}(u;t_*), r_{k,j}(u;t_*) \\
&\le \mu_{k,j}(S_k(t_*) + I_k(t_*) + R_k(t_*)),
\end{aligned} \tag{4}
$$

where we used $(IVT_{k,j})$. Using the definition of y, (4) implies that the inequality

$$
\begin{aligned}
0 &\le \big(y(u,0;y_0)\big)_1, \big(y(u,0;y_0)\big)_2, \big(y(u,0;y_0)\big)_3 \\
&\le (y_0)_1 + (y_0)_2 + (y_0)_3 \\
&\le \sqrt{3}\sqrt{((y_0)_1)^2 + ((y_0)_2)^2 + ((y_0)_3)^2}
\end{aligned}
$$

holds for $u \in [0,\infty)$, where $y_0 = \big((y_0)_1,(y_0)_2,(y_0)_3\big)^T$ is the initial value and we used the arithmetic-quadratic mean inequality. We conclude that the solution exists on $[0,\tau]$ and is bounded. ∎

Now we prove that if we assume that Λ_j and $\lambda_{k,j}$ possess the local Lipschitz property, then $\mathcal{F}$ is also locally Lipschitz continuous.

Lemma IV.2. *Let us suppose that for all $j,k \in \{1,\dots n\}$, Λ_j and $\lambda_{k,j}$ possess the local Lipschitz property, $\lambda_{k,j}(q_1,q_2,q_3) \ge 0$ and $\lambda_{k,j}(0,q_2,q_3) = 0$ hold for $q_1,q_2,q_3 \ge 0$. Then $\mathcal{F}$ satisfies the local Lipschitz condition on each bounded subset of $\mathcal{C}_+$.*

Proof: We claim that for every $M > 0$ there exists a constant $K = K(M)$ such that the inequality $|\mathcal{F}(\phi) - \mathcal{F}(\psi)| \le K\|\phi - \psi\|$ holds for every $\phi, \psi \in \mathcal{C}_+$ with $\|\phi\|, \|\psi\| \le M$.
Fix indices $j,k \in \{1,\dots n\}$. For $\|\psi\| \le M$ it holds componentwise that $0 \le \psi(-\tau_{k,j}) \le M$, so due to the continuity of $h_{k,j}$, there exists a constant $L^h_{k,j}(M)$ such that $0 \le h_{k,j}(\psi(-\tau_{k,j})) \le L^h_{k,j}$ is satisfied componentwise. For $y_0 = h_{k,j}(\psi(-\tau_{k,j}))$ Proposition IV.1 implies that there exists a $J_{k,j} = J_{k,j}(L^h_{k,j}) = J_{k,j}(M)$ such that the inequality $|\hat{y}_{\psi(-\tau_{k,j})}(u)| \le J_{k,j}$ holds for $u \in [0,\tau]$ (for instance we can choose $J_{k,j} = \sqrt{3}L^h_{k,j}$).
The local Lipschitz property of $h_{k,j}$ follows from its definition. We assumed that $\lambda_{k,j}$ is Lipschitz continuous, this implies the Lipschitz continuity of g. Let $K^h_{k,j} = K^h_{k,j}(M)$ be the Lipschitz constant of $h_{k,j}$ on the set $\{v \in \mathbb{R}^{3n} : |v| \le M\}$, we denote the Lipschitz constant of $g = g_{k,j}$ on the set $\{v \in \mathbb{R}^3 : |v| \le J_{k,j}\}$ by $K^g_{k,j} = K^g_{k,j}(J) = K^g_{k,j}(M)$. For any $\|\phi\|, \|\psi\| \le M$,

it holds that $|\phi(-\tau_{k,j})|, |\psi(-\tau_{k,j})| \le M$. Since solutions of (2) can be expressed as $y(u,0;y_0) = y_0 + \int_0^u g(y(r,0;y_0))\,\mathrm{d}r$, we have

$$
\begin{aligned}
&\big|\hat{y}_{\phi(-\tau_{k,j})}(u) - \hat{y}_{\psi(-\tau_{k,j})}(u)\big| \\
&= \bigg| h_{k,j}(\phi(-\tau_{k,j})) + \int_0^u g(\hat{y}_{\phi(-\tau_{k,j})}(r))\,\mathrm{d}r \\
&\quad - \bigg(h_{k,j}(\psi(-\tau_{k,j})) + \int_0^u g(\hat{y}_{\psi(-\tau_{k,j})}(r))\,\mathrm{d}r \bigg) \bigg| \\
&\le |h_{k,j}(\phi(-\tau_{k,j})) - h_{k,j}(\psi(-\tau_{k,j}))| \\
&\quad + \int_0^u \big|g(\hat{y}_{\phi(-\tau_{k,j})}(r)) - g(\hat{y}_{\psi(-\tau_{k,j})}(r))\big|\,\mathrm{d}r \\
&\le K^h_{k,j}\|\phi - \psi\| \\
&\quad + \int_0^u K^g_{k,j}\big|\hat{y}_{\phi(-\tau_{k,j})}(r) - \hat{y}_{\psi(-\tau_{k,j})}(r)\big|\,\mathrm{d}r
\end{aligned} \tag{5}
$$

for $u \in [0,\tau]$. Define

$$
\Gamma(u) = \big|\hat{y}_{\phi(-\tau_{k,j})}(u) - \hat{y}_{\psi(-\tau_{k,j})}(u)\big|
$$

for $u \in [0,\tau]$. Then (5) gives

$$
\Gamma(u) \le K^h_{k,j}\|\phi - \psi\| + K^g_{k,j}\int_0^u \Gamma(r)\,\mathrm{d}r,
$$

and from Gronwall's inequality we have

$$
\Gamma(u) \le K^h_{k,j}\|\phi - \psi\|e^{K^g_{k,j}u}. \tag{6}
$$

Applying the definition of W_k, we arrive to the inequality

$$
\begin{aligned}
&|(W_k(\phi))_j - (W_k(\psi))_j| \\
&= \big|\hat{y}_{\phi(-\tau_{k,j})}(\tau_{k,j}) - \hat{y}_{\psi(-\tau_{k,j})}(\tau_{k,j})\big| \\
&\le K^h_{k,j}e^{K^g_{k,j}\tau_{k,j}}\|\phi - \psi\|,
\end{aligned}
$$

where we used (6) at $u = \tau_{k,j}$.
It is straightforward that W_k has the Lipschitz condition for any $k \in \{1,\dots n\}$, $K^{W_k} = K^{W_k}(M) = \sqrt{\sum_{j=1}^n \big(K^h_{k,j}e^{K^g_{k,j}\tau_{k,j}}\big)^2}$ is a suitable choice for the Lipschitz constant.
Finally, the assumption that Λ_j is Lipschitz continuous for any $j \in \{1,\dots n\}$ implies the Lipschitz continuity of f, so let $K^f = K^f(M)$ be the Lipschitz constant of f on the set $\{v \in \mathbb{R}^{3n} : |v| \le M\}$. Then for any $\|\phi\|, \|\psi\| \le M$, $|\phi(0)|, |\psi(0)|, |\phi(-\tau)|, |\psi(-\tau)| \le M$ hold and thus

$$
\begin{aligned}
|\mathcal{F}(\phi) - \mathcal{F}(\psi)| &\le |f(\phi(0)) - f(\psi(0))| \\
&\quad + \sum_{k=1}^n |W_k(\phi) - W_k(\psi)| \\
&\le K^f\|\phi - \psi\| + \sum_{k=1}^n K^{W_k}\|\phi - \psi\|.
\end{aligned}
$$

$$|\Lambda_1(\mathbf{p}) - \Lambda_1(\mathbf{q})| = \beta_1 \left| \frac{q_1 q_2}{q_1 + q_2 + q_3} - \frac{p_1 p_2}{p_1 + p_2 + p_3} \right|$$

$$= \beta_1 \left| \frac{q_1 q_2}{q_1 + q_2 + q_3} - \frac{q_1 p_2}{q_1 + q_2 + q_3} + \frac{q_1 p_2}{q_1 + q_2 + q_3} \right.$$

$$- \frac{q_1 p_2}{q_1 + p_2 + q_3} + \frac{q_1 p_2}{q_1 + p_2 + q_3} - \frac{q_1 p_2}{q_1 + p_2 + p_3}$$

$$+ \frac{q_1 p_2}{q_1 + p_2 + p_3} - \frac{q_1 p_2}{p_1 + p_2 + p_3} + \frac{q_1 p_2}{p_1 + p_2 + p_3} - \frac{p_1 p_2}{p_1 + p_2 + p_3} \left. \right|$$

$$\leq \beta_1 \left(\left| \frac{q_1 q_2}{q_1 + q_2 + q_3} - \frac{q_1 p_2}{q_1 + q_2 + q_3} \right| \right.$$

$$+ \left| \frac{q_1 p_2}{q_1 + q_2 + q_3} - \frac{q_1 p_2}{q_1 + p_2 + q_3} \right| + \left| \frac{q_1 p_2}{q_1 + p_2 + q_3} - \frac{q_1 p_2}{q_1 + p_2 + p_3} \right| \tag{7}$$

$$+ \left| \frac{q_1 p_2}{q_1 + p_2 + p_3} - \frac{q_1 p_2}{p_1 + p_2 + p_3} \right| + \left| \frac{q_1 p_2}{p_1 + p_2 + p_3} - \frac{p_1 p_2}{p_1 + p_2 + p_3} \right| \left. \right)$$

$$= \beta_1 \left(|q_2 - p_2| \left| \frac{q_1}{q_1 + q_2 + q_3} \right| + |p_2 - q_2| \left| \frac{q_1 p_2}{(q_1 + q_2 + q_3)(q_1 + p_2 + q_3)} \right| \right.$$

$$+ |p_3 - q_3| \left| \frac{q_1 p_2}{(q_1 + p_2 + q_3)(q_1 + p_2 + p_3)} \right|$$

$$+ |p_1 - q_1| \left| \frac{q_1 p_2}{(q_1 + p_2 + p_3)(p_1 + p_2 + p_3)} \right| + |q_1 - p_1| \left| \frac{p_2}{p_1 + p_2 + p_3} \right| \left. \right)$$

$$\leq \beta_1 \left(2|q_2 - p_2| + |p_3 - q_3| + 2|p_1 - q_1| \right)$$

$$\leq 5\beta_1 |\mathbf{q} - \mathbf{p}|$$

Hence $K^f + \sum_{k=1}^{n} \sqrt{\sum_{j=1}^{n} \left(K_{k,j}^h e^{K_{k,j}^g \tau_{k,j}} \right)^2}$ is a suitable choice for K, the Lipschitz constant of $\mathcal{F}$ for the set $\{\psi \in \mathcal{C}_+ : ||\psi|| \leq M\}$. ∎

The assumptions of Lemma IV.2 on the incidences $\Lambda_j(S_j(t), I_j(t), R_j(t))$ and $\lambda_{k,j}(s_{k,j}(u; t_*), i_{k,j}(u; t_*), r_{k,j}(u; t_*))$ can be fulfilled by several choices on the type of disease transmission. For instance, let $\beta_j > 0$ be the transmission rate in region j and let $\beta_{k,j}^T > 0$ denote the transmission rates during travel. For $j, k \in \{1, \ldots n\}$ and for $\mathbf{q} = (q_1, q_2, q_3) \in \mathbb{R}^3$, define

$$\Lambda_j(\mathbf{q}) = -\beta_j \frac{q_1}{q_1 + q_2 + q_3} q_2,$$

$$\lambda_{k,j}(\mathbf{q}) = -\beta_{k,j}^T \frac{q_1}{q_1 + q_2 + q_3} q_2.$$

This implies that Λ_j and $\lambda_{k,j}$ have the form

$$\Lambda_j(S_j, I_j, R_j) = -\beta_j \frac{S_j}{N_j} I_j,$$

$$\lambda_{k,j}(s_{k,j}, i_{k,j}, r_{k,j}) = -\beta_{k,j}^T \frac{s_{k,j}}{n_{k,j}} i_{k,j}, \tag{8}$$

which is called standard incidence. Now we prove the following existence-uniqueness theorem.

Theorem IV.3. *With the incidences Λ_j and $\lambda_{k,j}$ defined in (8), there exists a unique solution of system (3).*

Proof: Recall Theorem 3.7 from [2]:

Suppose that $\mathcal{F}$ satisfies the local Lipschitz property on each bounded subset of $\mathcal{C}_+ = \mathcal{C}_+([-\tau, 0], \mathbb{R}_+^{3n})$, moreover let $M > 0$. There exists $A > 0$, depending only on M such that if $\phi \in \mathcal{C}_+$ satisfies $||\phi|| \leq M$, then there exists a unique solution $x(t) = \hat{x}(t, 0; \phi)$ of (3), defined on $[-\tau, A]$. In addition, if K is the Lipschitz constant for $\mathcal{F}$ corresponding to M, then

$$\max_{-\tau \leq \eta \leq A} |x(\eta, 0; \phi) - x(\eta, 0; \psi)| \leq ||\phi - \psi|| e^{KA}$$

holds for $||\phi||, ||\psi|| \leq M$.

We showed in Lemma IV.2 that the local Lipschitz continuity of $\mathcal{F}$ follows from the local Lipschitz property of the incidences and the nonnegativity condition of $\lambda_{k,j}$. The latter condition clearly holds, hence it is sufficient to prove that the incidences defined in (8) possess the local Lipschitz property.
As one may observe, the definition of the Λ_j-s and $\lambda_{k,j}$-

s ($j, k \in \{1, \ldots n\}$) only differ in a constant multiplier, hence it is sufficent to prove the local Lipschitz property only for one of them, i.e. for Λ_1. Moreover, we prove this property only on the nonnegative cone $\mathbb{R}^3_+$, which is invariant under systems (3) and (2). For $\mathbf{p}, \mathbf{q} \in \mathbb{R}^3_+$, by (7) we obtain the Lipschitz constant $K = 5\beta_1$, where we used that for any $a, b, c > 0$, it holds that $\frac{a}{a+b+c} < 1$. ∎

Remark 1. *It follows from the proof of Theorem IV.3 that the incidences Λ_j and $\lambda_{k,j}$ defined in (8) also satisfy the global Lipschitz property, meaning that the Lipschitz constant K arises independently of M. In this case, the solution of system (3) exists on $[0, \infty)$.*

Another natural choice for the incidences can be the following: for $\mathbf{q} = (q_1, q_2, q_3) \in \mathbb{R}^3$ and for $j, k \in \{1, \ldots n\}$, let

$$\Lambda_j(\mathbf{q}) = -\beta_j q_1 q_2,$$
$$\lambda_{k,j}(\mathbf{q}) = -\beta^T_{k,j} q_1 q_2,$$

which leads to the mass action-type disease transmission, therefore Λ_j and $\lambda_{k,j}$ have the form

$$\Lambda_j(S_j, I_j, R_j) = -\beta_j S_j I_j,$$
$$\lambda_{k,j}(s_{k,j}, i_{k,j}, r_{k,j}) = -\beta^T_{k,j} s_{k,j} i_{k,j}. \tag{9}$$

Theorem IV.4. *With incidences Λ_j and $\lambda_{k,j}$ defined in (9), there exists a unique solution of system (3).*

Proof: Similarly as by Theorem IV.3, it is enough to show that Λ_j and $\lambda_{k,j}$ satisfy the local Lipschitz property, we detail the proof only for Λ_1 and consider the nonnegative subspace R^3_+. For any $M > 0$, for any $\mathbf{p}, \mathbf{q} \in \mathbb{R}^3_+$ such that $|\mathbf{p}|, |\mathbf{q}| \le M$, we obtain

$$
\begin{aligned}
|\Lambda_1(\mathbf{p}) - \Lambda_1(\mathbf{q})| &= |-\beta_1 p_1 p_2 + \beta_1 q_1 q_2| \\
&\le \beta_1 |p_1 p_2 - q_1 q_2| \\
&\le \beta_1 |p_1 p_2 - p_1 q_2 + p_1 q_2 - q_1 q_2| \\
&\le \beta_1 (|p_1 p_2 - p_1 q_2| + |p_1 q_2 - q_1 q_2|) \\
&\le \beta_1 (p_1 |p_2 - q_2| + q_2 |p_1 - q_1|) \\
&\le 2M\beta_1 |\mathbf{q} - \mathbf{p}|,
\end{aligned}
$$

so we can choose $K(M) = 2M\beta_1$. ∎

Remark 2. *Although the global Lipschitz property does not hold for Λ_j and $\lambda_{k,j}$ defined in (9), it is possible to show that the solution of (3) is bounded and hence exists on $[0, \infty)$.*

V. CONCLUSION

The topic of epidemic spread of infectious diseases via transportation networks has recently been examined in several studies (see [3], [4], [5], [6], [7]), although these works mostly consider only two connected regions. We introduced a dynamic model which describes the spread of an infectious disease in and between n regions which are connected by transportation. We used the commonly applied SIR model as a basic epidemic building block in the regions and also during the travel. The model formulation led to a system structured by travel time, which turned out to be equivalent to a system of differential equations with multiple dynamically defined delays. We showed that under local Lipschitz conditions on the infection terms within the regions and during travel, the usual existence and uniqueness results hold.

Recent epidemics like the 2002-2003 SARS outbreak and the 2009 pandemic influenza A(H1N1) highlighted the importance of the global air travel network in the study of epidemic spread. During long distance travel such as intercontinental flights, a single infected individual may infect several other passengers during the flight, and since the progress of these diseases is fast, even a short delay (a fraction of a day) arising due to transportation may play a significant role in the disease dynamics. In this paper we illustrated by proving an existence and uniqueness result that such epidemiological situations can be studied in the framework of delay differential equations.

REFERENCES

[1] P. Hartman, "Ordinary differential equations", Classics in Applied Mathematics, vol. 38, SIAM, 2002.

[2] H. L. Smith, An Introduction to Delay Differential Equations with Applications to the Life Sciences, Springer, 2010.

[3] D. H. Knipl, "Fundamental properties of differential equation with dynamically defined delayed feedback", preprint, 2012.

[4] D. H. Knipl, G. Röst, J. Wu,"Epidemic spread of infectious diseases on long distance travel networks", preprint, 2012.

[5] J. Liu, J. Wu, Y. Zhou, "Modeling disease spread via transport-related infection by a delay differential equation", Rocky Mountain J. Math., vol. 38 No 5, pp. 1225–1541, 2008.

[6] Y. Nakata, "On the global stability of a delayed epidemic model with transport-related infection", Nonlinear Analysis Series B: Real World Applications, vol. 12 No 6, pp. 3028–3034 2011. http://dx.doi.org/10.1016/j.nonrwa.2011.05.004

[7] Y. Nakata, G. Röst, "Global analysis for spread of an infectious disease via global transportation", submitted, 2012.