MANAGEMENT EPIDEMICS USING HIGH COMPLEXITY MATHEMATICAL MODELING

PART II:
SEIMR/R-S
General Epidemic Simulation Model
Multi-Infected States - Multi Socio-Demographics Segments - Multi-Region Mobility

THEORY

Working Paper Version 1.5
Actual version: http://www.doanalytics.net/Documents/DW-2-ITM-SEIMR-R-S-Epidemic-Model-Theory.pdf

Jesus M. Velásquez-Bermúdez
Chief Scientist DecisionWare – DO Analytics
jesus.velasquez@decisionware.net

Laura Cruz, Hector Fraire, Alfredo Brambila
Nelson Rangel Valdez, Claudia Gomez
Instituto Tecnologico de México
hector.fraire.huacuja@itcm.edu.mx

Bogotá, December 2020

ABSTRACT

SEIMR/R-S corresponds to a generalized mathematical model of pandemics that enhances traditional, aggregated simulation models when considering inter-regional impacts in a macro region (conurbed); **SEIMR/R-S** also considers the impact of modeling the population divided into socio-demographic segments based on age and economic stratum (it is possible to include other dimensions, for example: ethnics, sex, …).

SEIMR/R-S is the core of the **SEIMR/R-S/OPT** epidemic management optimization model that determines optimal policies (mitigation and confinement) considering the spatial distribution of the population, segmented socio-demographically and multiple type of vaccines. The formulation of **SEIMR/R-S/OPT** is presented in **PART III: SEIMR/R-S/OPT Epidemic Management Optimization Model** (Velasquez-Bermudez 2021) describing its implementation in an optimization technology, like GAMS and AMPL. The modeling of the vaccination process is presented in Part III.

SEIMR/R-S can be understood and used by any epidemiologist, and/or physician, working with **SIR**, **SEIR** or similar simulation models, and by professionals working on the issue of public policies for epidemic control.

SEIMR/R-S epidemic model was carried out in a JAVA program. This program may be used by the organizations that considers the **SEIMR/R-S** will be useful for management the COVID-19 pandemic.

1. EPIDEMIC & CONTROL POLICIES MODEL

The **SEIMR/R-S** is a detailed epidemic model that is the result of integrating the **SIR**, **SEIR** and **SEI3RD** model; in these standard models the population is grouped in only one homogenous group. **SEIMR/R-S** extends the modeling to a multi-segment-sociodemographic multi-region system.

SEIMR/R-S model describes the epidemic with following states:

S **Susceptible:** initially covers all population that potentially can be infected (SU)

E **Exposed:** Population that has been infected and are in an incubation (latency) period (EX). The model SIR does not include this state.

IM **Multi-Infected:** Population that has been infected and has active the pathogen in different states of development (I0, I1,I2, … , IN). The active infected states are ordered according to the severity of the infection. The modeled SIR and SEIR consider only one infected state. For convenience, the last state is called "IN"

R **Recovered:** Recovering population (RE)

R-S is related with the Region-Segment model that considers multiples regions where live people classified in multiples socio-demographics segments.

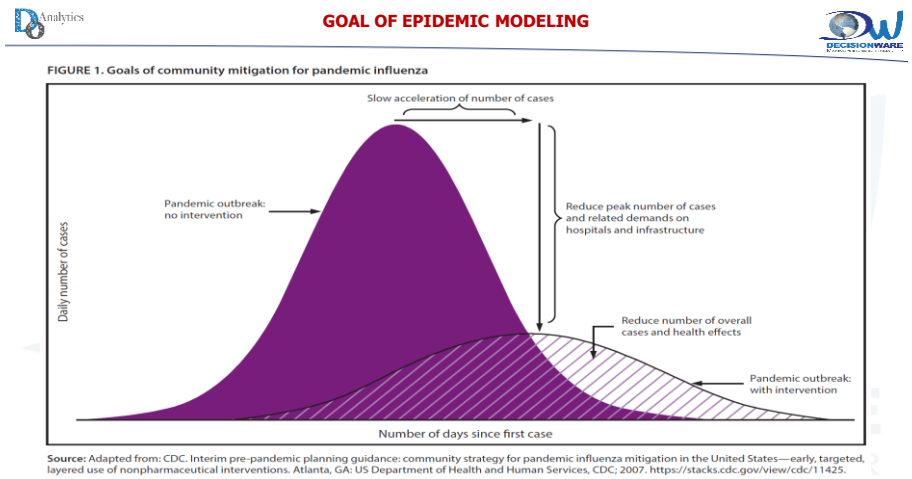
1.1. CONCEPTUAL FRAMEWORK

The following documents have been referenced and used for writing the following numerals:

- Brauer, F. and Castillo-Chavez, C. (2000). Mathematical Models in Population Biology and Epidemiology. Springer, New York, 2000.
- Cai, Y., Kang, Y., Banerjee, M., & Wang, W. (2015). A stochastic SIRS epidemic model with infectious force under intervention strategies. Journal of Differential Equations, 259(12), 7463-7502.
- Carcione, J., Santos J. E., Bagaini, C. and Jing, Ba. (2020) A Simulation of a COVID-19 Epidemic Based on a Deterministic SEIR Model.
- Erdem, M., Safan, M., & Castillo-Chavez, C. (2017). Mathematical analysis of an SIQR influenza model with imperfect quarantine. Bulletin of mathematical biology, 79(7), 1612-1636.

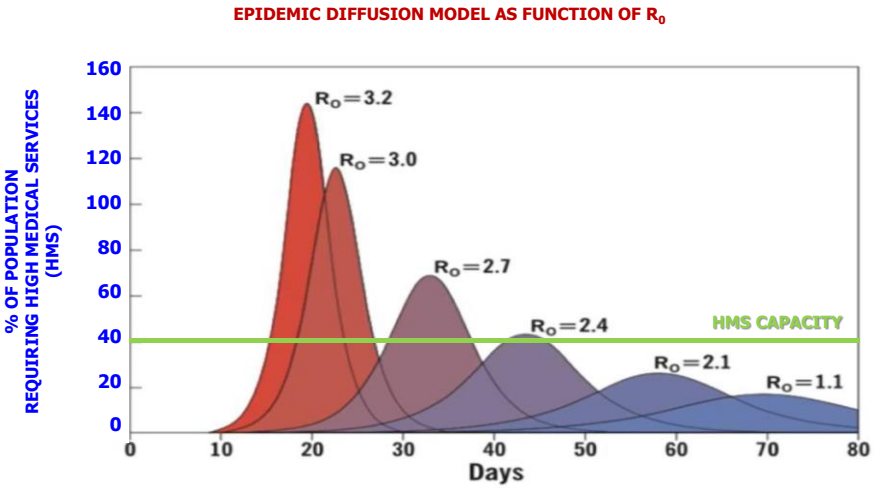
- Eubank, S., Eckstrand, I., Lewis, B., Venkatramanan, S., Marathe, M., & Barrett, C. L. (2020). Commentary on Ferguson, et al.,"Impact of Non-pharmaceutical Interventions (NPIs) to Reduce COVID-19 Mortality and Healthcare Demand". Bulletin of Mathematical Biology, 82, 1-7.
- Ferguson, N., Laydon, D., Nedjati Gilani, G., Imai, N., Ainslie, K., Baguelin, M., ... & Dighe, A. (2020). Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand.
- Hethcote, H. W. (2000). "The Mathematics of Infectious Diseases." SIAM Review 42.4 (2000), pp. 599–653.
- Huang G. (2016). Artificial infectious disease optimization: A SEIQR epidemic dynamic model-based function optimization algorithm. Swarm and evolutionary computation, 27, 31–67. https://doi.org/10.1016/j.swevo.2015.09.007
- Jing, W., Jin, Z., & Zhang, J. (2018). An SIR pairwise epidemic model with infection age and demography. Journal of biological dynamics, 12(1), 486-508.
- Kermack, W.O. and Mc Kendrick, A. G.,(1927) "Contributions to the Mathematical Theory of Epidemics, Part I". Proc. R. Soc. London, Ser. A, 115, 1927, 700-721.
- Liu M. and Liang, J. (2013). Dynamic optimization model for allocating medical resources in epidemic controlling. Journal of Industrial Engineering and Management JIEM, 2013 – 6(1):73-88 – Online ISSN: 2013-0953
- Massad, E., Bruattini, N.M., Coutinho, B. A. F. and Lopez, F. L., (2007). "The 1918 Influenza An Epidemic in the City" of Sao Paulo", Brazil, Medical Hypotheses, 68, 2007, 442-445
- Mejía Becerra, J. D. et. al. (2020). "Modelación Matemática de la Propagación del SARS-CoV-2 en la Ciudad de Bogotá. Documento de Circulación Informal
- Pang, W. (2020). Public Health Policy: COVID-19 Epidemic and SEIR Model with Asymptomatic Viral Carriers. Department of Mathematics and Statistics, McMaster University arXiv:2004.06311v1 [q-bio.PE] 14 Apr 2020.
- Radulescu, A., & Cavanagh, K. (2020). Management strategies in a SEIR model of COVID 19 community spread. arXiv preprint arXiv:2003.11150.
- Samsuzzoha, Md. (2012) . "A Study on Numerical Solutions of Epidemic Models". Doctoral Thesis, Swinburne University of Technology, Australia, 2012.

The goal of epidemic control strategies is to reduce R_0. This can be achieved by reducing susceptibility or contact rates in the population or the infectiousness of infected populations. The potential effectiveness of medical intervention by varying the infectiousness of infected populations and nonmedical interventions by reducing the contact rates in the population have been examined. In medical intervention, use of vaccines and/or antiviral agents for case of treatment can increase the recovery rate and reduce the death rate. On the other hand, in nonmedical interventions, reducing population contact rates through social distancing and travel restrictions can reduce the impact on the transmission process.



Control of an outbreak relies partly on identification of the disease parameters that lead to a significant reduction of the basic reproduction number $\mathbf{R_0}$ that may be function of several parameters of which γ,

the recovery rate for clinically ill and β, the transmission coefficient, are the most sensitive parameters. These two parameters can be controlled by medical intervention and nonmedical interventions.



The modeling of epidemics in a solidly developed area of scientific knowledge, widely studied based on simulation models. The master table of epidemic models shows some of the best-known models

TABLE: MAE_EMO			
STATE (COD_EMO)	**DESCRIPTION (DIN_EMO)**	**Reference (COM_EMO)**	**Imple mented**
SIR	Susceptibility (S), Infection (I) and Recovery (R)	Kermack & Mc Kendrick (1927) Jing (2018)	YES
SEIR	Susceptibility (S), Exposure (E), Infection (I) and Recovery (R)	Hethcote (2000)	YES
SEIRA	Susceptibility (S), Exposure (E), Infection (I) and Recovery (R)		NOT
SEI3RD	Susceptibility (S), Exposure (E), 3+1 Infection States (I3), Recovery (R) and Death (D)	Mejía Becerra et. al. (2020)	YES
SEIQR	Susceptibility (S), Exposure (E), Infection (I), Quarantine (Q) and Recovery (R)	Huang (2016)	NOT
SIRS	Susceptibility (S), Infection (I), Recovery (R) and Susceptibility (S)	Cai (2015)	NOT

Then, an epidemiological model is defined based on differential equations that explain the evolution of the process without human intervention. These differential equations can be established based on the population (number of people) who are in a certain "epidemic" state or based on the fraction of the population that is in that state. The epidemic models are nonlinear systems of ordinary differential equations, traditionally this equations system is solved using simulation models based in a discrete approximation for continuous derivatives, be it over time or space. There are many possible schemes. These models are used to analyze several widely discussed (predefined) scenarios and provide evidence on their effectiveness and are not oriented to get the optimal solution of a mix of control policies.

The added value by mathematical programming approach is to convert simulation models into optimization models to be able to combine them with other mathematical programming models, following the principles of structured mathematical modeling that allows join multiple problems of mathematical programming in a single model. Based on the above, the formulation of the models is done by means of algebraic equations that represent how the epidemiological process evolves during the planning horizon.

For the optimization epidemic modeling, the approach is based on multiple state chains that can be associated with semi-Markov chains; initially, it was proposed to model based on the approach of semi-Markovian processes (changing transition matrices over time) but such an approach brings multiple complications in the math formulation of probabilities.

After analyzing the implementation of main (most known) epidemiological models (SIR, SEIR), it was decided to directly model discrete versions of differential equations as they maintain direct connection with biological parameters, which facilitates the connection of these parameters with socio-demographic segments.

Therefore, all epidemiological models considered should be formulated in one of the following terms.

- The time unit of the differential equations is one day.
- The states contain the fraction of the population in each state.
- The time of the optimization model may be divided in periods of multiple days (one week, seven days). In this case, the integration of the differential equations must be made using calculated parameters.

The epidemic states are showed in the master table **MAE_STA**. The models will be implemented using this nomenclature. The table includes the symbol used in the original models and the code used in the information system to reference the state.

EPIDEMIC STATES - TABLE: MAE_STA			
MODEL SYMBOL	**EPIDEMIC STATE (COD_STA)**	**DESCRIPTION (DIN_STA)**	**COMMENTS (DLIN_STA)**
S	SU	Susceptible Population	Those individuals who have not been exposed to the pathogen and are susceptible to being infected by it.
E	EX	Exposed Population	Those individuals who are in the latency state; that is, they have been inoculated by the pathogen but are not yet infectious
I	IN	Infected Population	In SIR and SEIR models is infected population. It must be the most critical state for infected people; this is important for models that have more than one epidemic states to describe the infection process.
I_0	I0	Asymptomatic Infectious	Those individuals in the population who have been inoculated by the virus are infectious but have not developed symptoms. Those infected in this state rarely learn that they have been infected.
I_1	I1	Moderate Symptoms Infectious	Those individuals in the population who are infectious and have mild or moderate symptoms. They are those who can be given management of the disease at home.
I_2	I2	Severe Symptoms Infectious	Those individuals in the population who are infectious and have severe but not critical symptoms. Individuals present in this state require hospitalization.
I_3	IN	Critical Symptoms Infectious	It must be the most critical state for infected people; this is important for models that have more than one epidemic states to describe the infection process. In SIR and SEIR models is infected population
R	RE	Recovered Population	Those individuals recover from infection, having developed antibodies. In most of the models they cannot be re-infected.
	ED	Epidemic Dead	Individuals who fail the infection and die.
	ND	Natural Dead	Individuals who die by other reason different to the epidemic
	NP	New Population	Individuals coming from an exogenous macro-region.

The indexes used in the modeling are presented in the next table.

INDEXES		
Index HEA	**Short Description (Entities)**	**Long Description**
ag	Age	Age
mr	Macro-region	Macro-Region
rg, ro, rd	Region	Region (Basic Territory Unit)
ss	Social Segment	Socio-Demographic Segment
st, s1	Epidemic State	Epidemic State
t, q	Period	

The measurements used must be equal for all models

Measurement Unit Master Table: MAE_UND	
Measurement Unit COD_UND	**Description DES_UND**
1/peo-day	1/ persons-day

Measurement Unit Master Table: MAE_UND	
Measurement Unit COD_UND	**Description DES_UND**
fpo/day	Fraction of population per day
peo-day	Persons-day

One of the main limitations of the traditional approach is to assume that the entire population is homogeneous with respect to its epidemiological behavior. It is well known that the epidemic manifests differently in each socio-demographic stratum and that the composition of socio-demographic segments depends on each region.

In order to enhance the model to be useful in real cases, it is assumed that there is a different pandemic (because it has different parameters) for each pair <region, demographic-segment. These hypotheses may vary according to each case study. In this case, reference has been made to the data used to control the epidemic in a macro-region. It should be noted that the parameters of each epidemiological model vary in quantity but do not vary in the form of calculation, since they are parameters as the same case, which is studied with different mathematical models.

The models are studied under the hypothesis of a homogeneous population in a region, then the epidemic is assumed to be particular to each duple <rg,ss> and the equations are formulated depending on <rg,ss>. The advantage of this approach will be visualized when the epidemic model is coupled with the management of health resources and control policies, which can be individualized for each duple <rg,ss>.

The model parameters can be grouped by the original source of variation, these sources are:
- Pathogen: characteristics of the epidemic due to the pathogen
- Age: It is typical for recovery/worsening times (rates) and probability of recovery to be a function of age.
- Economic stratum: influences the epidemic by means of the intensity of contact, product of the number of contacts, the duration of contacts and the closeness, these variables may also be a combined function of age and economic.

Additionally, may be considered people coming for the exogenous systems (out of the microregion) to the region.

In this case, the socio-demographic segments are a combination of age with an economic stratum. The biological parameters depend on age.

2. GENERAL SIMULATION EPIDEMIC MODEL

Below is presented an aggregate model of epidemic that is the result of integrating the **SIR** model, **SEIR** and **SEI3RD**; in these standard models the population is grouped in only one homogenous group. **SEIMR/R-S** extends the modeling to a multi-segment-sociodemographic multi-region system.

The general assumptions for standard epidemic models are:
- No vaccine exists
- The susceptible population is reduced through infection (moving to infective state).
- People who recovered after catch the virus will be insusceptible of it
- The population of infective class is increased by a fraction of susceptible individuals becoming infective.
- All other people are susceptible
- The population is homogenous
- The population of "critical" infective individuals is reduced by recovery from the disease.

SEIMR/R-S model describes the epidemic with following states:

S **Susceptible:** initially covers all population that potentially can be infected (SU)

E **Exposed:** Population that has been infected and are in an incubation (latency) period (EX). The model SIR does not include this state.

IM **Multi-Infected:** Population that has been infected and has active the pathogen in different states of development (I0, I1,I2, … , IN). The active infected states are ordered according to the severity of the infection. The modeled SIR and SEIR consider only one infected state. For convenience, the last state is called "IN"

R **Recovered:** Recovering population (RE)

R-S is related with the Region-Segment model that considers multiples regions where live people classified in multiples socio-demographics segments.

The next table shows the relation between models and epidemic states.

Model	SEIMR/R-S Model Epidemic States												
	Standard								Extended			Capacity	
	SU	EX	I_0	I_1	I_2	...	I_N	RE	NP	ED	ND	IU	CD
SIR	x						x	x					
SEIR	x	x					x	x					
SEI3RD	x	x	x	x	x	x	x	x		x			
SEIMR/R-S	x	x	x	x	x	x	x	x	x	x	x	x	x

2.1. SIR: EPIDEMIC MODEL

The **SIR** model is a basic model in epidemic modeling (Kermack and Mc Kendrick, 1927). **SIR** process, starting with a susceptible host who becomes infected, the class of infection grow for the infected individuals to be able to transmit the infection to susceptible. When the infected individual is no longer able to transmit infection to susceptible individual, the infected individual is removed from the cycle of diseases transmission in the population. This model is based on the following assumption:

Then, the basic **SIR** model describes the epidemic with three states:

S Susceptible: initially covers all population that potentially can be infected **(SU)**

I Infected: Population that has been infected (IN)

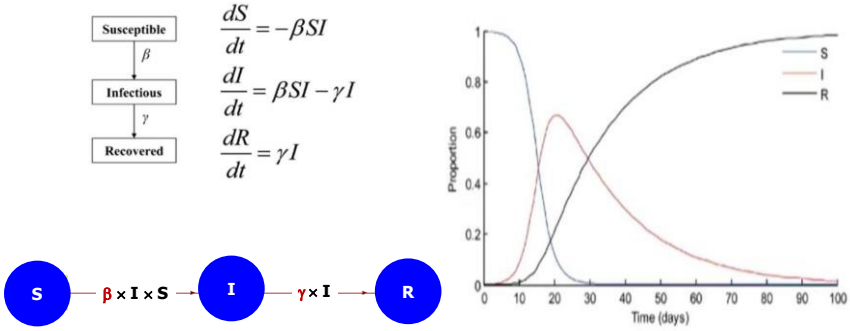
R Recovered: Recovering population (RE)

The diagram shows the behavior of **S(t)**, **I(t)**, and **R(t)** when they are normalized to total of population (**TPOB**) equal to 1. The biological parameters used in SIR and SEIR model are described below.

SIR MODEL - BIOLOGICAL PARAMETERS			
Parameter	**Description**	**Equation**	**Measure Unit**
δ	Contact Intensity – Exogenous Parameter		peo-day
ω	Probability of transmission per contact intensity (infectivity)		
γ	Recovery rate for clinically ill		fpo/day
μ	Epidemic death (mortality) rate		fpo/day
μ^N	Natural mortality rate		fpo/day
κ	The latency period of the virus before developing		day
ψ	Inverse virus latency period	$1/\kappa$	$1/\kappa$
β	Inverse contact intensity $\times$ infectivity	$\delta\delta \times \omega$	$\delta\delta \times \omega$
ρ	Relative removal rate	γ/β	
R_0	Basic reproduction ratio/number		

The diagram resumes the standard SIR epidemic model.

Susceptible-Infectious-Recovered (SIR)
Epidemic Model



SIR model is represented based on three differential equations based on proportions of people in each state (the ratio between the people in a state with the initial population **TPOB**). The measurements between parentheses.

$$\partial \mathbf{S(t)}/\partial \mathbf{t}\ \text{(fpo/day)} = -\ \beta\ \text{(1/fpo-day)} \times \mathbf{I(t)}\ \text{(fpo)} \times \mathbf{S(t)}\ \text{(fpo)}$$

$$\partial \mathbf{I(t)}/\partial \mathbf{t}\ \text{(fpo/day)} = \beta\ \text{(1/fpo-day)} \times \mathbf{I(t)}\ \text{(fpo)} \times \mathbf{S(t)}\ \text{(fpo)} - \gamma\ \text{(fpo/day)} \times \mathbf{I(t)}\ \text{(fpo)}$$

$$\partial \mathbf{R(t)}/\partial \mathbf{t}\ \text{(fpo/day)} = \gamma\ \text{(fpo/day)} \times \mathbf{I(t)}\ \text{(fpo)}$$

where **S(t)**, **I(t)**, **R(t)** represent the population of susceptible, infected, and recovered individuals, respectively. Adding these equations, the following condition must be hold

$$\partial \mathbf{S(t)}/\partial \mathbf{t} + \partial \mathbf{I(t)}/\partial \mathbf{t} + \partial \mathbf{R(t)}/\partial \mathbf{t} = \mathbf{0}$$

Additionally, **SIR** can be extended with other epidemic states for a more complete description of the system/epidemic:

NP New population entering the system, as people from abroad who in many cases are the ones who cause the epidemic (NP).

ED People who die due to the epidemic (these people die regardless of the management of the epidemic (D).

ND People who die from natural death (N)

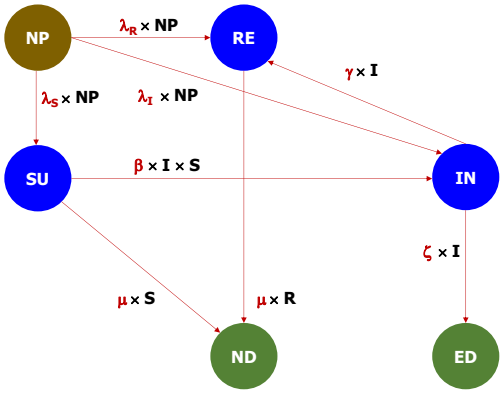
ND and **ED** states should be included if it wants to account for the resources consumed by people who die, who are killed due the epidemic and due by causes other than the epidemic.

For a more general formulation it is included the exogenous variable **NPX(t)** tha represents the proportion of people arriving from an exogenous system, may be births or people arriving from a foreign country/region. The value of **NPX(t)** is a border condition with the foreign system over any value of **t** it is calculated taking as reference the initial population **TPOB**. This adjustment may be important in regions high people exchange rates islands dedicated to tourism. Next table shows the parameters used to this modeling.

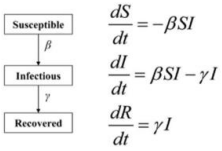
EXOGENOUS SYSTEM PARAMETERS		
Parameter	**Description**	**Measure Unit**
λ^E	Exposed rate coming from the exogenous system	fpo/day
λ^S	Susceptible rate coming from the exogenous system	fpo/day
λ^I	Infectious rate coming from the exogenous system	fpo/day
λ^R	Recovered rate coming from the exogenous system	fpo/day

Next diagram shows the epidemic system modeled.

STATE TRANSITION DIAGRAM - SIR MODEL



STATE	DESCRIPTION
NP	New Population
SU	Susceptive Population
IN	Infective Population
RE	Recovered Population
ND	Natural Dead
ED	Epidemic Dead



Then, the differential SIR equations must be adjusted:

$$\partial S(t)/\partial t = - \beta \times I(t) \times S(t) + \lambda^S \times NPX(t) - \mu^N \times S(t)$$

$$\partial I(t)/\partial t = \beta (I(t) \times S(t) - (\gamma + \zeta) \times I(t) + \lambda^I \times NPX(t)$$

$$\partial R(t)/\partial t = \gamma \times I(t) - \mu^N \times R(t) + \lambda^R \times NPX(t)$$

$$\partial D(t)/\partial t = \mu \times I(t)$$

$$\partial N(t)/\partial t = \mu^N \times S(t) + \mu^N \times R(t)$$

where μ^N represents the natural mortality rate and λ^{st} the rates coming from the exogenous system to the state st.

If **TPOB** is the initial total population, and it is constant over time, **NPX(t)=0**, the model meets the hypothesis that at all times

$$\mathbf{S(t) + I(t) + R(t) + D(t) + N(t) = 1}$$

If **NPX(t)** is different from zero the previous equation must be adjusted as

$$\mathbf{S(t) + I(t) + R(t) + D(t) + N(t) = 1 + \int_{q\in[0,t]} \partial NPX(q)\, \partial q}$$

To simulate the process the border conditions at the beginning of the simulation horizon are: **S(0), I(0), R(0), D(0)** and **NPX(t),** for all **t.**

Assuming **NPX(t)** equal to zero, the ratio $\rho = \gamma/\beta$ is called the relative removal rate. Thus, dynamics of infectious depends on the following ratio:

$$\mathbf{R_0 = S(0) \times \gamma/\beta}$$

where $\mathbf{R_0}$, called the basic reproduction ratio/number, is defined as the number of secondary infections produced by a single infectious individual during his/her entire infectious period. The role of the basic reproduction number is especially important. However, the following mathematical analysis describes how the basic reproduction number depends on the host population and the infected host.

At time **t = 0**, $\partial I/\partial t$ can be written as

$$\mathbf{\partial I/\partial t = (R_0 - 1) \times \gamma \times I(0)}$$

if $\mathbf{R_0} > 1$ then $\partial \mathbf{I}/\partial \mathbf{t} > 0$ and therefore the disease can spread; but if $\mathbf{R_0} < 1$ then the disease dies out. Making mathematical manipulation it is possible to prove that the maximum number of infective at any time is

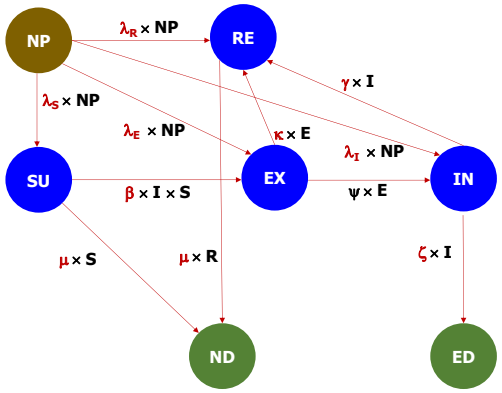
$$\mathbf{TPOB\ (1 - \rho + \rho\ ln\ [\ \rho\ /\ S(0)\ ]\ )}$$

It should be noted that the probability of transition becomes a dynamic variable that must be calculated by the mathematical model, for that reason the **t** index must be included.

2.2. SEIR EPIDEMIC MODEL

The classic SEIR model describes the epidemic dynamics based on the transitions between four different compartments (epidemic states): susceptible (S), exposed (E), infectious (I), and recovered (R) individuals. The SEIR symbols are the same SIR symbols plus the parameter ψ that represents the inverse of the virus latency/incubation period (κ). There are multiple versions of the SEIR model, below are some images summarizing some of the literature consulted: Radulescu & Cavanagh (2020), Hethcote, H. W. (2000), Carcione et a. (2020), Pang, W. (2020), Liu and Liang (2013), Grimm et al. (2020).

STATE TRANSITION DIAGRAM - SEIR MODEL



STATE	DESCRIPTION
NP	New Population
SU	Susceptive Population
EX	Exposed Population
IN	Infective Population
RE	Recovered Population
ND	Natural Dead
ED	Epidemic Dead

$$\frac{dS}{dt} = -\beta IS,$$
$$\frac{dE}{dt} = \beta IS - \varepsilon E,$$
$$\frac{dI}{dt} = \varepsilon E - \gamma I,$$
$$\frac{dR}{dt} = \gamma I,$$

The equations of **SEIR** model are the same as those of **SIR** model considering the following changes:

$$\partial E(t)/\partial t = \beta \times I(t) \times S(t) - \psi \times E(t) + \lambda^E \times NPX(t)$$

$$\partial I(t)/\partial t = \psi \times E(t) - (\gamma + \zeta) \times I(t) + \lambda^I \times NPX(t)$$

2.3. SEIMR EPIDEMIC MODEL

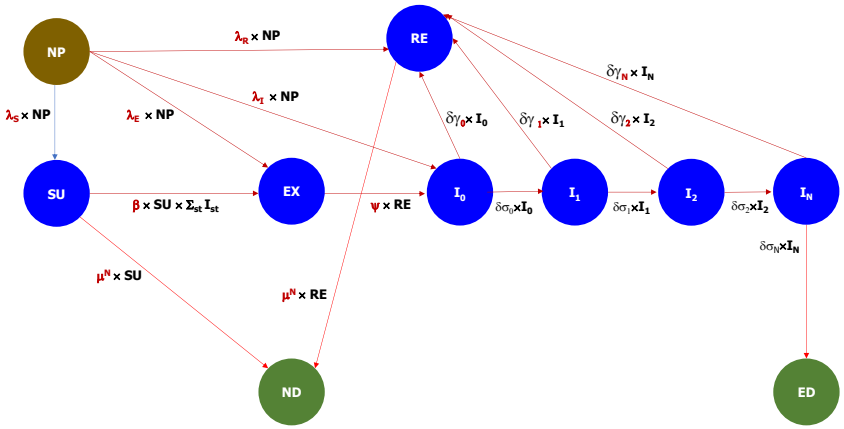
SEIMR is a generalization of the **SEI3RD** epidemic model that was developed with the aim of simulating the transmission and evolution of acute infections. This simulation assumes that the pathogen causes an infection followed by lifelong immunity or death. Two versions of **SEI3RD** was revised: Grimm et al. (2020) and Mejía Becerra et al. (2020), this version is used in this document.

In **SEI3RD** models the classic **SEIR** model is extended to distinguish between:

i) Several categories of infectiousness; for example: asymptomatic, symptomatic, moderate, and severe cases
ii) Recovered and dead people.

Being able to explicitly distinguish these different groups is important as they can greatly differ in terms of their underlying parameters as well as in terms of their behavioral response to public health interventions compared with the **SEIR** Model.

STATE TRANSITION DIAGRAM – SEI3RD / SEIMRD EPIDEMIC MODELS



The transition between infected states follows this assumptions:

- A person can only be infected by one of the individuals belonging to one of the infected states (I_0, I_1, I_2, I_3, … , I_N). In advance, it will be used the index **st** that is equivalent to index **i**.
- Being inoculated by the pathogen, the individual passes to the group of exposed E.
- After the latency period, the person in the exposed state becomes asymptomatic infectious (I_0 state).
- Once the person is in I_{st} state, there are two possible outcomes: worsening clinical status (moving to mild/moderate/critical infected I_{st+1}) or recovery (R).
- If the person recovers, in any of the states of infection, they enter the absorbent recover state (R).
- Similar logic applies for a larger number of states of infection. It is understood that if an individual of the last state of infection (I3) worsens its clinical condition if it die (E).

Next table shows the biological parameters of **SEI3RD** epidemic model.

BIOLOGICAL PARAMETERS – SEI3RD MODEL			
Parameter	**Description**	**Equation**	**Measure Unit**
μ^N	Natural mortality rate		fpo/day
κ	The latency period of the virus before developing		day
μ	Epidemic mortality rate		fpo/day
ω	Probability of that a person may be contagion		prob
δ_{st}	Probability of I_0, I_1, I_2, I_3, … of recovering		prob
π_{st}	Time a patient in I_0, I_1, I_2, I_3, … recovers		day
η_{st}	Time a patient in I_0, I_1, I_2, I_3, … to next infected state		day
ζ_{st}	Total contact free rate in I_1, I_2, I_3, …		1/day
c_{st}	Free probability of contagion in state I_1, I_2, I_3, …		Prob
γ_{st}	Fraction of people who recover in one day	$1/\pi_{st}$	fpo/day
σ_{st}	Fraction of people who develops symptoms	$1/\eta_{st}$	fpo/day
β_{st}	I_0, I_1, I_2, I_3, … state transmissibility free rate	$-\zeta_{st}\, log(1 - c_{st})$	fpo/day
ψ	Inverse virus latency period	$1/\kappa$	1/day

It should be noted that there are differences in the equations related to transmissibility rate between the formulation presented by Mejía Becerra et al. (2020) and the standard formulations for SIR and SEIR models. This aspect will be analyzed a later numeral.

It is important to understand the relationship between the probability of recovery, the recovery/worsening time, and the rate of departure of people from a state. The output rate from one state to another state may be based on the following expression:

Output Rate to State (st) = Output Probability to State (st) / Departure Time to State (st)

The total exit rate to any state implies the sum of exit rates to all states.

$$\text{Output Rate} = \Sigma_{st} \text{ Output Rate to State (st)}$$

The **SEI3RD** equations (Mejía Becerra et al., 2020) of the dynamic model described previously symbolize the proportion of individuals in the population in each of the states (S, E, I_i, R and D), they are:

$$\partial S(t)/\partial t = - S(t) (\beta_0(t) \times I_0(t) + \beta_1(t) \times I_1(t) + \beta_2 \times I_2(t) + \beta_3 \times I_3(t))$$

$$\partial E(t)/\partial t = S(t) (\beta_0(t) \times I_0(t) + \beta_1(t) \times I_1(t) + \beta_2 \times I_2(t) + \beta_3 \times I_3(t)) - \psi \times E(t)$$

$$\partial I_0(t)/\partial t = \psi \times E(t) - \delta_0 \times \gamma_0 \times I_0(t) - (1 - \delta_0) \times \sigma_0 \times I_0(t)$$

$$\partial I_1(t)/\partial t = (1 - \delta_0) \times \sigma_0 \times I_0(t) - \delta_1 \times \gamma_1 \times I_1(t) - (1 - \delta_1) \times \sigma_1 \times I_1(t)$$

$$\partial I_2(t)/\partial t = (1 - \delta_1) \times \sigma_1 \times I_1(t) - \delta_2 \times \gamma_2 \times I_2(t) - (1 - \delta_2) \times \sigma_2 \times I_2(t)$$

$$\partial I_3(t)/\partial t = (1 - \delta_2) \times \sigma_2 \times I_2(t) - \delta_3 \times \gamma_3 \times I_3(t) - (1 - \delta_3) \times \sigma_3 \times I_3(t)$$

$$\partial R(t)/\partial t = \delta_0 \times \gamma_0 \times I_0(t) + \delta_1 \times \gamma_1 \times I_1(t) + \delta_2 \times \gamma_2 \times I_2(t) + \delta_3 \times \gamma_3 \times I_3(t)$$

$$\partial D(t)/\partial t = (1 - \delta_3) \times \sigma_3 \times I_3(t)$$

The following specification must be considered:

1. ψ is the reciprocal of the average latency period.

2. δ_{st} is the likelihood (probability) that an individual in group I_{st} will recover without worsening their clinical condition. This version of SERI3D considers that the people only death, for epidemic reasons, in the last infected state. This limitation may be relaxed but it implies the estimation of more parameters. Then, μ the mortality rate is equal to $\delta_{st,}$ for st equal to the last infected state.

3. γ_{st} is the reciprocal of the average recovery time, without worsening its clinical state, of an individual of class I_{st}.

4. σ_{st} is the reciprocal of the average complication time of a patient in the I_{st} state.

5. β_{st} is the transmissibility rate of an individual in state I_{st}. Mejía Becerra et al. (2020) includes transmissibility rates related with the epidemic control policies, this is ignored in **SEIMR/R-S** general formulation, but it will be presented later in the MBC case.

Then, the equations of **SEI3RD** model are the same as those of the previous **SEIR** model considering the following changes:

$$\partial S(t)/\partial t = - [\Sigma_{st \in INF} \beta_{st} \times I_{st}(t)] \times S(t) + \lambda^S \times NPX(t) - \mu^N \times S(t)$$

$$\partial E(t)/\partial t = [\Sigma_{st \in INF} \beta_{st} \times I_{st}(t)] \times S(t) - \psi \times E(t) + \lambda^E \times NPX(t)$$

$$\partial I_0(t)/\partial t = \psi \times E(t) - \delta\delta_0 \times I_0(t) + \lambda^I \times NPX(t)$$

$$\partial I_{st}(t)/\partial t = \delta\sigma_{st-1} \times I_{st-1}(t) - \delta\delta_{st} \times I_{st}(t)$$

$$\partial R(t)/\partial t = \Sigma_{st \in INF} \delta\gamma_{st} \times I_{st}(t) - \mu^N \times R(t) + \lambda^R \times NPX(t)$$

$$\partial D(t)/\partial t = \Sigma_{st \in IF} \delta\sigma_{st} \times I_{st}(t)$$

The following relations should be considered:

- Equation $\partial \mathbf{I_{st}(t)/\partial t}$ valid for st$\in$I1F (the set of infected states excluding the first infected state, I_0)

- $st \in INF$ is the set of all infected states
- $st \in IF$ is the set associated to the last infected state.

The following definitions (auxiliary parameters) was included

$$\sigma\delta_{st} = \delta_{st} \times \sigma_{st}$$
$$\delta\sigma_{st} = (1 - \delta_{st}) \times \sigma_{st} = \sigma_{st} - \sigma\delta_{st}$$
$$\delta\gamma_{st} = \delta_{st} \times \gamma_{st}$$
$$\delta\delta_{st} = (\delta_{st} \times \gamma_{st} + (1 - \delta_{st}) \times \sigma_{st}) = \delta\gamma_{st} + \delta\sigma_{st}$$
$$\mu = \Sigma_{st \in IF}\, \delta\sigma_{st}$$

The following table resumes the equation included in SEIMR model. The equation has been divided in positive (increment) and negative (decrement) impacts on the state st.

SEIMR - Differential Equations				
$st \in SET$	State Increment	State Decrement	Natural Dead	Exogenous Increment
SU	$\lambda^S \times NPX(t)$	$IS(t) \times S(t)$	$\mu^N \times S(t)$	$\lambda^S \times NPX(t)$
EX	$IS(t) \times S(t)$	$\psi \times E(t)$		$\lambda^E \times NPX(t)$
IN	$IS(t) \times S(t)$	$\delta\delta_{st} \times I_{st}(t)$		$\lambda^I \times NPX(t)$
I0	$\psi \times E(t)$			$\lambda^I \times NPX(t)$
I1F	$\delta\sigma_{st-1} \times I_{st-1}(t)$			
RE	$\Sigma_{st \in I1F}\, \delta\gamma_{st} \times I_{st}(t)$		$\mu^N \times R(t)$	$\lambda^R \times NPX(t)$
ED	$\Sigma_{st \in IF}\, \mu \times I_{st}(t)$			
	AUXILIARY EQUATION			
	$IS(t) = [\ \Sigma_{st \in INF}\, \beta_{st}(t) \times I_{st}(t)\ ]$			

These equations serve to represent any of the three models studied. The conditions are as follows:

1. SIR Model:
   - Only consider one infected state IN the definitions of the infected state sets are: $st \in IF=\{IN\}$, $st \in I1F=\{\}$, $st \in I0=\{\}$, $st \in INF=\{IN\}$ and $st \in IN=\{IN\}$
   - Do not include the exposed state (E), that means that $st \in EX=\{\}$
2. SEIR Model
   - Only consider one infected state IN the definitions of the infected state sets are equal to SIR model.
3. SEIMR Model
   - Considered multiples infected stats {I0, I1, I2,… , IN} IN associate to I_N, do not include the state I_0 that means: $st \in IF=\{I_N\}$, $st \in I1F=\{I_1, I_2, \dots, I_N\}$, $st \in I0=\{I_0\}$, $st \in INF=\{I_0, I_1, I_2, \dots, I_N\}$ and $st \in IN=\{I\}$

The next table presents the SETs of epidemic states needed to model the three epidemics models. The infected sets permit to model any of the three models with the same equations; they are used to define the existence conditions of the equations and in summation limits into the equations.

Epidemic States SETs											
Model	Epidemic States	Non Infected States					Infected States				
	STA	SU	EX	RE	ED	ND	INF	IN	I0	I1F	IF
SIR	S, I, R, D, N	S		R	D	N	I	I			
SEIR	S, E, I, R, D, N	S	E	R	D	N	I	I			
SEIMR	S, E, I_0, I_1, I_2, … , I_N, D, N	S	E	R	D	N	I_0, I_1, I_2, … , I_N		I_0	I_1, I_2, … I_{N-1}	I_N

3. SEIMR/R-S GENERAL EPIDEMIC MODEL

The **SEIMR/R-S** model is built on the basic equations of the **SEIMR** model including the effects of considering the development of the epidemic in a territory (macro-region) that includes multiple regions in which the population socio-demographic segments are distributed in a non-homogeneous manner.

3.1. COMMON ALGEBRAIC NOTATION

Including regional and socio-demographic segment modeling (in this case age and economic stratum) involves associating the biological parameters with these aspects. Therefore, biological parameters may be related to indices: rg (region), ss (socio-demographic segment), ag (age) and/or se (economic stratum).

The next table shows the basic parameters of the **SEIMR** and **SEIMR/R-S** and their relationships.

BIOLOGICAL PARAMETERS – SEI3RD & SEIMR/R-S Models				
SEIMR	**SEIMR/R-S**		**Description**	**Measure Unit**
Parameter	**Parameter**	**Source**		
μ^N	μ^N	Read	Natural mortality rate	fpo/day
κ	κ	Read	The latency period of the virus before developing	day
μ	μ_{ag}	Model	Epidemic mortality rate	fpo/day
ω	$\omega_{rg,ss}$	Model	Probability of that a person may be contagion	prob
δ_{st}	$\delta_{ag,st}$	Model	Probability of I_0, I_1, I_2, I_3, ... of recovering	prob
π_{st}	$\pi_{ag,st}$	Model	Time a patient in I_0, I_1, I_2, I_3, ... recovers	day
η_{st}	$\eta_{ag,st}$	Model	Time a patient in I_0, I_1, I_2, I_3, ... to next infected state	day
β_{st}	β	Model	Transmissibility rate of an individual in state st	
ζ_{st}	ζ	Model	Total contact free rate in I_1, I_2, I_3, ...	1/day
c_{st}	$c_{ag,st}$	Model	Free probability of contagion in state I_1, I_2, I_3, ...	prob

The source **Model** indicates that parameters should be the result of the mathematical model of parameters to be constructed from the regional distribution of socio-demographic segments and their characterization from specific studies developed for the macro-region. This topic will be discussed in detail in the implementation of the City of Bogotá (Velásquez, 2020).

Because the variability of the **SEI3RD** parameters is simpler than that of the **SEIMR/R-S** parameters it is possible to replace the **SEIMR/R-S** parameters with the **SEIMR** to have an equivalent model, but less explanatory of the details that differentiate the epidemic process in the regions.

The calculated biological parameters used in **SEIMR/R-S** model is presented below; they are divided in basic and auxiliary parameters that are included to make easier the implementation process.

BIOLOGICAL PARAMETERS (CALCULATED) - SEIMR/R-S MODEL					
SEIMR		**SEIMR/R-S**		**Description**	**Measure Unit**
Parameter	**Equation**	**Parameter**	**Equation**		
γ_{st}	$1/\pi_{st}$	$\gamma_{ag,st}$	$1/\pi_{ag,st}$	Fraction of people who recover in one day	fpo/day
σ_{st}	$1/\eta_{st}$	$\sigma_{ag,st}$	$1/\eta_{ag,st}$	Fraction of people who develops symptoms	fpo/day
β_{st}	$-\xi_{st}\log(1-c_{st})$	β_{st}	$-\xi_{st}\log(1-c_{ag,st})$	I_0, I_1, I_2, I_3, ... state transmissibility rate	fpo/day
ψ	$1/\kappa$	ψ	$1/\kappa$	Inverse virus latency period	1/day
$\sigma\delta_{st}$	$\delta_{st}\,\sigma_{st}$	$\sigma\delta_{ag,st}$	$\delta_{ag,st}\,\sigma_{ag,st}$	$\delta_{ag,st}\,\sigma_{ag,st}$	
$\delta\sigma_{st}$	$(1-\delta_{st})\,\sigma_{st}$	$\delta\sigma_{ag,st}$	$(1-\delta_{ag,st})\,\sigma_{ag,st}$	$(1-\delta_{ag,st})\,\sigma_{ag,st}$	
$\delta\gamma_{st}$	$\delta_{st}\,\gamma_{st}$	$\delta\gamma_{ag,st}$	$\delta_{ag,st}\,\gamma_{ag,st}$	$\delta_{ag,st}\,\gamma_{ag,st}$	
$\delta\delta_{st}$	$\delta\gamma_{st}+\delta\sigma_{st}$	$\delta\delta_{ag,st}$	$\delta\gamma_{ag,st}+\delta\sigma_{ag,st}$	$\delta\gamma_{ag,st}+\delta\sigma_{ag,st}$	
μ	$\Sigma_{st\in IF}\,\delta\sigma_{st}$	μ_{ag}	$\Sigma_{st\in IF}\,\delta\sigma_{ag,st}$	$\Sigma_{st\in IF}\,\delta\sigma_{ag,st}$	
		$\beta\rho_{rg,ss}$	Model	Contagion probability function of regional and socio-demographics characteristics	prob
		$\beta\beta_{rg,ss}$	$\Sigma_{ag\in AGS(ss)}\,\delta\delta_{ag,st}\times\beta\rho_{rg,ss}$	Inverse contact intensity × infectivity	1/fpo-day

3.2. REGIONAL-SEGMENT MODELING

3.2.1. REGIONAL MODELING

To formulate the regional model segmented socio-demographically the following hypotheses are assumed:

- There is no contagion between people living in different regions. This can be true for large regions such as states or departments. But it is questionable for metropolitan areas (cities and conurbed regions) where there is intense traffic between regions.

- The inter-region interrelationship is modeled on the following assumptions:
  - There is traffic of people between regions, which sets for each pair of regions the fraction of each segment, $\varphi_{ro,rg,ss}$, moving from the source region (ro) to the destination region (rg).
  - In addition, the fraction of the time, $\phi_{ro,rg,ss}$, is known to people from the region origin in the destination region during the period (one day).

The calculation process involves determining the impact on the spread of the virus that the population movement has for this purpose it is calculated using the number of infected people who can move between two regions multiplied by the fraction of the time spent in the destination locality. This implies the following effects on the diffusion rate:

1. Infected Movements

   - Increasing the rate of diffusion in the destination locality due to those infected by coming from other regions, it is calculated as:

$$\mathbf{II_{rg}(t)} = \Sigma_{ss\in SSR(rg)} \Sigma_{ro\in ROR(rg)} \varphi_{ro,rg,ss} \times \phi_{ro,rg,ss} \times \mathbf{IS_{ro,ss}(t)}$$

   - Decreased diffusion rate in the source region due to the infected by moving to other regions, it is calculated as:

$$\mathbf{IE_{rg}(t)} = \Sigma_{ss\in SSR(rg)} \Sigma_{rd\in RDE(rg)} \varphi_{rg,rd,ss} \times \phi_{rg,rd,ss} \times \mathbf{IS_{rg,ss}(t)}$$

     The net effect on the rg-region will be:

$$\mathbf{IS_{rg,ss}(t)} = \Sigma_{st\in INF} \mathbf{I_{st,rg,ss}(t)}$$

$$\mathbf{IX_{rg}(t)} = \Sigma_{ss\in SSR(rg)} \mathbf{IS_{rg,ss}(t)}$$

$$\mathbf{IR_{rg}(t)} = \mathbf{IX_{rg}(t)} + \mathbf{II_{rg}(t)} - \mathbf{IE_{rg}(t)}$$

     where

$\mathbf{I_{st,rg,ss}(t)}$	fraction of the population infected in st-epidemic-state living in rg-region and ss-segment.
$\mathbf{IS_{rg,ss}(t)}$	fraction of the population infected living in rg-region and ss-segment.
$\mathbf{IX_{rg}(t)}$	fraction of the population infected living in rg-region
$\mathbf{II_{rg}(t)}$	weighted fraction of the population infected traveling to rg-region
$\mathbf{IE_{rg}(t)}$	weighted fraction of the population infected traveling from rg-region

2. Susceptible Movements

   - Increasing the rate of diffusion in the destination locality (rg-region) due to those susceptible people by coming from other regions that may be infected in rg-region, it is calculated as:

$$\mathbf{SI_{ro,rg,ss}(t)} = \varphi_{ro,rg,ss} \times \phi_{ro,rg,ss} \times \mathbf{S_{ro,ss}(t)}$$

     The following replace of parameter will be included

$$\varphi\phi_{ro,rg,ss} = \varphi_{ro,rg,ss} \times \phi_{ro,rg,ss}$$

   - Decreased diffusion rate in the source region (rg-region) due to the susceptible people by moving to other regions that cannot be infected in rg-region, it is calculated as:

$$\mathbf{SE_{rg,rd,ss}(t) = \varphi\phi_{rg,rd,ss} \times S_{rd,ss}(t)}$$

The susceptible population living in the rg-region ss-segment must be decremented by the susceptible people belonging to other regions:

$$\mathbf{SN_{rg,ss}(t) = S_{rg,ss}(t) - \Sigma_{rd \in RDE(rg)}\, SE_{rg,rd,ss}(t)}$$

where

$S_{rg,ss}(t)$ fraction of the susceptible population living in rg-region and ss-segment.

$SI_{ro,rg,ss}(t)$ fraction of the ss-segment susceptible population traveling from ro-region to rg-region

$SE_{rg,rd,ss}(t)$ fraction of the ss-segment susceptible population traveling from rg-region to rd-region

Next table resume the parameters associated with regional modeling

REGIONAL MODELING PARAMETERS – SEIMR/R-S MODEL			
Parameter	**Source / Equation**	**Description**	**Measure Unit**
$\varphi_{ro,rg,ss}$	Model	Fraction of ss-segment population moving from the source region (ro) to the destination region (rg)	fpo/day
$\phi_{rg,rd,ss}$	Model	Fraction time that spends the ss-segment population of the source region (ro) into the destination region (rg)	hour/day
$\varphi\phi_{rg,rd,ss}$	$\varphi_{rg,rd,ss} \times \phi_{rg,rd,ss}$	$\varphi_{rg,rd,ss} \times \phi_{rg,rd,ss}$	hour/day

3.2.2. SOCIO DEMOGRAPHIC SEGMENT MODELING

An infected person in any segment can infect anyone susceptible in any socio-demographic segment.

The calculation process implies that at the level of one region the population of any segment can infect the population of any other segment. To do this, diffusion (infection of susceptible from infected) is managed at a detailed level in the differential equations for all infected states, but in the differential equation the infected transmission is calculated based on the summation of all infected states in all ss-segments.

In traditional aggregated models, this the transfer rate β (the inverse of contact intensity multiplied by the transmission probability) is assumed fixed for all region and all socio demographics segments. In **SEIMR/R-S** the transfer rate depends on the socio-demographic segment in a region and it is called $\beta\beta_{rg,ss}$, this parameter must be calculated by the parameters model.

Then, the contagion of the susceptible population living in the rg-region and belonging to the ss-segment will be the sum of the contagions that occur in the rg-region (people that do not travel out of the rg-region) plus the contagions that occur in the rd destination regions this is

$$\mathbf{S2I_{rg,ss}(t) = \beta\beta_{rg,ss} \times IR_{rg}(t) \times SN_{rg,ss}(t) + \Sigma_{rd \in RDE(rg)}\, \beta\beta_{rd,ss} \times IR_{rd}(t) \times SE_{rg,rd,ss}(t)}$$

3.3. GENERAL FRAMEWORK

The differential equations of the regional-segmented model are:

$$\partial S_{rg,ss}(t)/\partial t = - S2I_{rg,ss}(t) - \mu^N \times S_{rg,ss}(t) + \lambda^S{}_{rg,ss} \times NPX(t)$$

$$\partial E_{rg,ss}(t)/\partial t = S2I_{rg,ss}(t) - \psi \times E_{rg,ss}(t) + \lambda^E{}_{rg,ss} \times NPX(t)$$

st=I0

$$\partial I_{st,rg,ss}(t)/\partial t = \psi \times E_{rg,ss}(t) - \delta\alpha_{st,ss} \times I_{st-1,rg,ss}(t) + \lambda^I{}_{rg,ss} \times NPX(t)$$

st∈I1F

$$\partial I_{st,rg,ss}(t)/\partial t = \delta\zeta_{st-1,ss} \times I_{st-1,rg,ss}(t) - \delta\alpha_{st,ss} \times I_{st,rg,ss}(t)$$

$$\partial R_{rg,ss}(t)/\partial t = \Sigma_{st\in I1F}\, \delta\beta_{st-1,ss} \times I_{st,rg,ss}(t) - \mu^N \times R_{rg,ss}(t) + \Sigma_{ss\in SSR(rg)}\, \lambda^R{}_{rg,ss} \times NPX(t)$$

$$\partial D_{rg,ss}(t)/\partial t = \Sigma_{st\in I1F}\, \mu\sigma_{ss} \times I_{st,rg,ss}(t)$$

$$\partial NR_{rg}(t)/\partial t = \mu^N \times SR_{rg,ss}(t) + \mu^N \times RR_{rg}(t)$$

where the following rates are defined for the socio-demographic segments

SOCIO-DEMOGRAPHIC BIOLOGICAL PARAMETERS		
Parameter	Equation	Description
$\delta\alpha_{st,ss}$	$\Sigma_{ag\in AGS(ss)}\, \delta\delta_{ag,st}$	Total exit rate
$\delta\zeta_{st,ss}$	$\Sigma_{ag\in AGS(ss)}\, \delta\sigma_{ag,st}$	Worsening exit rate
$\delta\beta_{st,ss}$	$\Sigma_{ag\in AGS(ss)}\, \delta\gamma_{st,ag}$	Recovering exit rate
$\mu\sigma_{ss}$	$\Sigma_{ag\in AGS(ss)}\, \mu_{ag}$	Mortality rate depending on segment
μ_{ag}	$\Sigma_{st\in I1F}\, \delta\sigma_{ag,st}$	Mortality rate depending on age

The definition equations of the regional-segmented model are:

$$IS_{rg,ss}(t) = \Sigma_{st\in INF}\, \beta_{st,rg,ss}(t)\, I_{st,rg,ss}(t)$$
$$IX_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, IS_{rg,ss}(t)$$
$$II_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, \Sigma_{ro\in ROR(rg)}\, \varphi\phi_{ro,rg,ss} \times IS_{ro,ss}(t)$$
$$IE_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, \Sigma_{rd\in RDE(rg)}\, \varphi\phi_{rg,rd,ss} \times IS_{rg,ss}(t)$$
$$IR_{rg}(t) = IX_{rg}(t) + II_{rg}(t) - IE_{rg}(t)$$

$$SR_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, S_{rg,ss}(t)$$
$$SI_{ro,rg,ss}(t) = \varphi\phi_{ro,rg,ss} \times S_{ro,ss}(t)$$
$$SE_{rg,rd,ss}(t) = \varphi\phi_{rg,rd,ss} \times S_{rd,ss}(t)$$
$$SN_{rg,ss}(t) = S_{rg,ss}(t) - \Sigma_{rd\in RDE(rg)}\, SE_{rg,rd,ss}(t)$$
$$SIN_{rg}(t) = \beta\beta_{rg,ss} \times IR_{rg}(t) \times SN_{rg,ss}(t)$$
$$SIE_{rg,ss}(t) = \Sigma_{rd\in RDE(rg)}\, \beta\beta_{rd,ss}\, IR_{rd}(t) \times SE_{rg,rd,ss}(t)$$
$$S2I_{rg,ss}(t) = SIN_{rg}(t) + SIE_{rg}(t)$$

$$RR_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, R_{rg,ss}(t)$$

$$DR_{rg}(t) = \Sigma_{ss\in SSR(rg)}\, D_{rg,ss}(t)$$

From now on, the above mathematical definitions will be summarized as

$$\mathbf{\{\, S, E, I_{st}, D, N \,\} \in \Theta}$$

The next table shows the equations dividing the increment and the decrement on each state, it must be considered in the implementation of the mathematical models. The table includes the sets that defined the existence of the equations manly for the infected states.

	SIR Regional – Segmented Model - Differential Equations				
Set	State	State Increment	State Decrement	Natural Dead	Exogenous Increment
	REGIONAL - SEGMENT EQUATIONS				
SU	$\partial S_{rg,ss}(t)/\partial t$		$S2I_{rg,ss}(t)$	$\mu^N \times S_{rg,ss}(t)$	$\lambda^S{}_{rg,ss} \times NPX(t)$
EX	$\partial E_{rg,ss}(t)/\partial t$	$S2I_{rg,ss}(t)$	$\psi \times E_{rg,ss}(t)$		$\lambda^E{}_{rg,ss} \times NPX(t)$
I0	$\partial I_{st,rg,ss}(t)/\partial t$	$\psi \times E_{rg,ss}(t)$	$\delta\alpha_{st,ss} \times I_{st,rg,ss}(t)$		$\lambda^I{}_{rg,ss} \times NPX(t)$
I1F	$\partial I_{st,rg,ss}(t)/\partial t$	$\delta\zeta_{st-1,ss} \times I_{st-1,rg,ss}(t)$			
RE	$\partial R_{rg,ss}(t)/\partial t$	$\Sigma_{st\in I1F}\, \delta\beta_{st,ss} \times I_{st,rg,ss}(t)$		$\mu^N \times R_{rg,ss}(t)$	$\lambda^R{}_{rg,ss} \times NPX(t)$
ED	$\partial D_{rg,ss}(t)/\partial t$	$\Sigma_{st\in I1F}\, \mu\sigma_{ss} \times I_{st,rg,ss}(t)$			
ND	$\partial NR_{rg}(t)/\partial t$	$\mu^N \times (SR_{rg}(t) + RR_{rg}(t))$			
	SUSCEPTIBLE STATE EQUATIONS				

	SIR Regional – Segmented Model - Differential Equations				
Set	State	State Increment	State Decrement	Natural Dead	Exogenous Increment
	$SR_{rg}(t) = \Sigma_{ss \in SSR(rg)} S_{rg,ss}(t)$				
	$SI_{ro,rg,ss}(t) = \varphi\phi_{ro,rg,ss} \times S_{ro,ss}(t)$				
	$SE_{rg,rd,ss}(t) = \varphi\phi_{rg,rd,ss} \times S_{rd,ss}(t)$				
	$SN_{rg,ss}(t) = S_{rg,ss}(t) - \Sigma_{rd \in RDE(rg)} SE_{rg,rd,ss}(t)$				
	$SIN_{rg,ss}(t) = \beta\beta_{rg,ss} \times IR_{rg}(t) \times SN_{rg,ss}(t)$				
	$SIE_{rg,ss}(t) = \Sigma_{rd \in RDE(rg)} \beta\beta_{rd,ss} IR_{rd}(t) \times SE_{rg,rd,ss}(t)$				
	$S2I_{rg,ss}(t) = SIN_{rg}(t) + SIE_{rg}(t)$				
	INFECTED STATE EQUATIONS				
	$IS_{rg,ss}(t) = \Sigma_{st \in INF} \beta_{st,rg,ss}(t) I_{st,rg,ss}(t)$				
	$IX_{rg}(t) = \Sigma_{ss \in SSR(rg)} IS_{rg,ss}(t)$				
	$II_{rg}(t) = \Sigma_{ss \in SSR(rg)} \Sigma_{ro \in ROR(rg)} \varphi\phi_{ro,rg,ss} \times IS_{ro,ss}(t)$				
	$IE_{rg}(t) = \Sigma_{ss \in SSR(rg)} \Sigma_{rd \in RDE(rg)} \varphi\phi_{rg,rd,ss} \times IS_{rg,ss}(t)$				
	OTHER EQUATIONS				
	$RR_{rg}(t) = \Sigma_{ss \in SSR(rg)} R_{rg,ss}(t)$				
	$DR_{rg}(t) = \Sigma_{ss \in SSR(rg)} D_{rg,ss}(t)$				

4. FUNDING

This project is funding by DecisionWare, by CONACYT (Consejo Nacional de Ciencia y Tecnología de México) and by ITCM (Instituto Tecnologico de Ciudad Madero).