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Platform for European Medical Support During Major Emergencies

D3.1 Context Models

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PULSE

Platform for European Medical Support during major emergencies

WP3MODELLING

Deliverable D3.1 Context Models

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Responsible:	Organisation:	Contributing WP:
Alessandro Borri	UCSC	WP3

Authors (organisation)
Alessandro Borri (UCSC)
Eleonora Pacciani (UCSC)
Andrea De Gaetano (UCSC)

Abstract:

The purpose of this document is to provide a supporting document for the software prototypes of Deliverable D3.1 “Context Models” of WP3 “Modelling”.
The document describes the basic layer of models and algorithms representing the simulation engine of the integrated Decision Support System (DSS), which is the end-product of PULSE. The implemented simulation modules simulate the evolving situation, either starting with arbitrary conditions, or carrying forward currently observed field conditions.
D3.1 covers the following tasks of WP3:

- T3.1: Design and test of the patient model.
- T3.2: Design and testof health care effect model.
- T3.3: Design and test of health care facilities model.
- T3.6: Design and test of applicable event evolution models for biological events.

By means of the integrated suite of models, the system will provide the simulation engine for the WP4 Tools.
The models are accessible as webservices, which constitute the core of the modeling prototypes. For the purpose of the present deliverable, a synthetic client in the form of a Graphical User Interface (GUI) has been designed for testing the connection to the webservices and to perform basic tests on a subset of functionalities. Parameter tuning and implementation refinements are the object of future deliverables, as described in the final part of the document.

Keywords:

Model, Stadium Crush scenario, SARS scenario, Physiological State Variables, SEIR model, patient evolution, epidemics evolution.

D3.1-Context Models - REVISIONS:

Revision	Date	Description	Author (Organisation)
0.1	23/07/2015	Preliminary draft	UCSC
0.2	29/07/2015	Restructured draft incorporating some suggestions from the Rome technical meeting (28/7/2015)	UCSC
1.0	31/08/2015	Final draft	UCSC

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1 Glossary

Table 1: Glossary

Term	Definition	Notes (examples from PULSE, explanations. ...)
DoW	Document of Work	The official document, version 2013-10-11, that states PULSE project scope and content
ECDC	European Center of Desease Prevention and Control	
Ethical issues	Ethical issues refer to the issues concerning some aspect that raise ethical questions	
GUI	Graphic User Interface	
IHR	International Health Regulations The International Health Regulations (2005) are legally binding regulations (forming international law) that aim to a) assist countries to work together to save lives and livelihoods endangered by the spread of diseases and other health risks, and b) avoid unnecessary interference with international trade and travel	
LMS	A Learning Management System is a software application for the administration, documentation, tracking, reporting and delivery of e-learning education courses or training programs. LMS typically are accessible through a standard web browser from which the courses being managed can be accessed and taken.	In PULSE, the LMS system will store and deliver training courses to the different categories of end users.
LRS	Learning Record Store. A Learning Record Store (LRS) stores learning records, allows reporting against the records, and allows for exporting of raw learning data.	
Methodology	in PULSE project, methodologies are mainly procedures which will be adequate to improve the operation and success of the healthcare system in challenging disaster situations where combined operations are required at local, regional, cross border and international levels	
MIC	Medical Incident Commander MIC key task is to coordinate and organise the medical resources at the scene of an incident allocating tasks and roles	
Model (see also PULSE Model)	An abstraction of reality with the aims of better understanding it, mostly described in mathematical/ analytical, also sociological or philosophical terms and methodologies	
MPORG	MultiPlayer Online Role Playing Game are popular for both training and recreational gaming. People typically use an avatar to represent themselves in a virtual world where they can perform tasks in predefined scenarios. Multiple people participate and interact in the same virtual world in parallel. MPORG system are typically accessed via the internet and used by end users in disparate locations.	Within PULSE an MPORG system and environment will be used to train personnel within the stadium crush scenario where individuals will assume the roles of different resource personnel involved in such a scenario.
Phase	A subset of a Scenario. It may be, for instance, identified, for instance, in terms of time (e.g. before the incident) and/or location (e.g. Hospital) and/or type of population involved(e.g. people in "uncertain" status in a SARS like epidemic), and/or purpose (prepare, recover)	Each PULSE Scenario is split in two Phases: Preparedness and Response.
Platform	see *PULSE Platform*	
PMA	Posto Medico Avanzato	
Preparedness phase	Activities that prepare and train responders and ensure that the needed mix of resources are ready to respond in case of adverse event	
Response phase	Activities that are triggered by the adverse event, with the purpose to diminish/contain its effects	
SARS	Severe Acute Respiratory Syndrome	
SARS-like	Infectious respiratory desease	
Scenario	Description of an incident in terms of background, occurrence and the course of a incident, including response and other related processes of relevance	In PULSE we consider two Scenarios: SARS-like epidemics and Stadium crush-like incident
SOP	Standard Operational Procedures	SOPs may have different levels of detail: e.g. Policy, Actor/Activity tables, Procedures
Tactical Preparedness sub-phase	Activities that prepare the response to a specific adverse event ; the sub-phase starts when the situation that may generate the event is announced and ends when the event happens or the situation is no more in place. Lesson learning after the end of the response phase are included in the Tactical Preparedness sub-phase.	In Stadium Scenario the sub-phase may start when the authorization for the concert is asked.
Tool	Any helping software instrument, including input/output interfaces with users or other Tools or Systems (mostly software). A Tool may use PULSE Models. A software Tool may also be identified with a set of functionalities.	PULSE Platform includes 8 Tools.
WHO	World Health Organization	

2 Introduction

2.1 Purpose of the Document

The goal of the present document is to support the prototype (software) deliverable D3.1 – Context Models of PULSE Work Package 3 “Modelling”.

The software part of the deliverable follows a client-server architecture; it consists of an archive file, containing a JAR (Java Archive) client, calling models and algorithms which are available in form of webservices on the CNR-IASI server running from the UCSC Gemelli Hospital.

The PULSE Platform is showcased mainly by two basic scenarios: a Stadium Crush Scenario, representing cases of trauma incidents, and a SARS Scenario, covering the issues related to the epidemics evolution. Such scenarios have been extensively described in the WP2 deliverables. The suite of WP3 models and algorithms constitute the basic layer in the simulation engine of the PULSE Decision Support System (DSS), to be fully developed in the second part of the project.

2.2 Scope of the Document

This document summarizes the software component delivery and provides high level details on the models, software architecture and underlying technologies on which the software component has been developed.

With respect to the DoW, the present deliverable covers the following tasks:

- T3.1: Patient model (Stadium Crush scenario).The patient model calculates the effects of injuries of several victims. The model interacts with the scenario generation to calculate the severity and kind injury (physical trauma).
- T3.2: Health care effect model (Stadium Crush scenario).This model simulates the first aid personnel activities in case of crisis. The model interacts with the patient model (T3.1) and the health care facilities model (T3.3) to calculate and forecast the evolution of the patient health status according with the level of care in the field and in the definitive care structures.
- T3.3:Health care facilities model (Stadium Crush scenario and SARS scenario).This model describes the hospital capacity, health care effect, hospital surge capability and timing. In this way, the imbalance between optimal care needs, resources availability and any on-going reductions in the levels of both will be quantifiable.
- T3.6: Evolution models for biological events (SARS scenario).This model

simulates the epidemics evolution. It is an extended version of the classical SIR (Susceptible – Infectious – Recovered) and SEIR (Susceptible – Exposed-Infectious - Recovered) models.

In this prototype deliverable, the model implementations are described as stand-alone functions and tested separately in a subset of their functionalities. In the future deliverable D3.2 “Scenario generation”, the models will be conducted in an integrated simulation and the related functions will be fed with data generated by the Scenario generator.

2.3 Structure of the Document

The main features and funtionalities of the models are described in Section 3, in natural language and by means of mathematical formalism, independently of the programming language in which the models are actually implemented. Section 4 describes the architecture of the system, in particular the client-server architecture, a description of the client interface and of the functions which are used to implement the model, with particular focus on the number and type of input and output parameters. Section 5 describes the technologies underlying the software implementation, including external libraries. Section 6 offers concluding remarks about the future test and validation processes and the relationship of the present deliverable with other deliverables and work packages.

3 Main features and functionalities

3.1 Basic features

The implementation of the models in PULSE follows two distinct approaches for the modelling of individuals in the two PULSE scenarios:

- Stadium Crush scenario (trauma incidents): the patient will be modeled by means of continuous physiological variables; the state of the system can assume infinitely many values.
- SARS scenario (epidemics event): each individual can assume one over 4 possible states: Susceptible, Exposed, Infectious, Recovered.

Accordingly, the patient evolution in PULSE considers two different evolution schemes in the two PULSE scenarios:

- Stadium Crush scenario (trauma incidents): the evolution of the patient is governed by sets of Ordinary Differential Equations (ODEs) which determine the continuous “trajectory” of the physiological variables.
- SARS scenario(epidemics event): the epidemics evolution is based on a deterministic and spatially distributed mean-value model; the rate at which the population of each terrain cell changes its state within the next time step depends on the state of the neighbors.

3.2 Detailed functionalities

3.2.1 Patient model (T3.1 Stadium Crush scenario)

The goal is the assessment of the evolution of patient health status with respect to evolving time, modeling the effects of injuries of several types on civilian victims.The Stadium Crush Scenario produces a certain number of “affected” individuals among the existing “bystanders”, producing on each individual a set of anatomical lesions (with different severity) from a given library. Each anatomical lesion occurs with specified probability distribution (Table 2 specifying the estimated probability of occurrence of each lesion in this type of scenario). The Lesion library contains the following physical trauma lesions:

- Head/neck;
- Face;
- Chest;

- Abdomen;
- Extremities;
- External.

Table 2: Estimated probability of occurrence of each lesion in the Stadium Crush scenario

Scenario/lesions probability	Head/Neck	Face	Chest	Abdomen	Extremities	External
Stadium crush	20%	10%	80%	30%	40%	20%

In turn, the anatomical lesions determine the occurrence of physiological defects along some physiological dimensions (ten of these are currently considered). In agreement with the ABCDE Primary Survey and Resuscitation, there are only five main ways to die, from fatal complications involving: Airways (A), Breathing (B), Circulation (C), Disability of Nervous System (D), Extra Damage or Exposure (E). Accordingly, the patient dynamics can be described by a set of (normalized) physiological variables (0 is the minimum or deadly and 1 is the maximum or healthy value), based on the ABCDE paradigm:

- A1: airway patency (intact, at risk, partially obstructed, or completely obstructed);
- B1: respiratory rate and drive;
- B2: tidal volume and mechanics;
- B3: oxygen saturation and transport;
- C1: heart pump function;
- C2:circulation filling and resistances;
- D1:central nervous System Function(Glasgow Coma Scale, GCS);
- D2: seizures;
- D3: cholinergic activity;
- E1: exposure, hypothermia, burns.

The patient model predicts the evolution over time of the above mentioned physiological dimensions (or variables).The evolution is determined by the initial variable status (the initial defect) and the initial rate of worsening. Table 3 reports the list of the physiological variables along with their description and an example of a damage causing a defect in them.

Table 3: Description of the physiological variables

Variable name	Description	Example of a case determining a defect in the variable
A1	Airway patency	Neck trauma
B1	Respiratory rate and drive	Head trauma
B2	Tidal volume and mechanics	Chest trauma
B3	Oxygen saturation and transport	CO intoxication (smoke, fire)
C1	Heart pump function	Wound to the mediastinum
C2	Circulation filling and resistances	Blood loss
D1	Central nervous System Function	Head trauma
D2	Seizures	Head wound
D3	Cholinergic activity	Noxious gas inhalation
E1	Exposure, hypothermia, burns	Fire

The mathematical model describes the physiological patient evolution in terms of piecewise-linear trajectories in the state space. The evolution is governed by sets of Ordinary Differential Equations (ODEs), which determine the "trajectory" of the physiological variables. In the normal form of first order, the evolution of each variable satisfies the following differential equation:

$$\frac{\mathrm{dx(t)}}{\mathrm{d}t} = -\alpha \qquad t \geq t_0 \qquad (1)$$

starting from the initial condition:

$$x(t_0) = 1 - \Delta \qquad (2)$$

where:

- t_o is the start of the event;
- x(t) is the value assumed by each physiological variable at time $t \geq t_o$, when the damage of each variable starts. Each variable takes values in [0,1], where 1 is the initial healthy value, and has a lower-bound value under which the patient's health is compromised;
- $x(t_o)$ is the value assumed by each physiological variable at time $t = t_o$;
- dx(t)/dt = v(t) is the speed at which each variable changes its state;
- Δ: $\Delta \in [0,1]$ is the maximal initial damage at time t_o;
- α: $\alpha \in \mathbb{R}_o+$ is the maximal worsening rate [relative damage/unit time].

At time $t=t_0$, the event starts affecting the patient's status at (possibly) different times for each individual, causing lesions: the patient functionalities have a sudden relative damage Δ; then they decrease at a rate α. The values (Δ,α) are different for each patient (according to their severity) and for each physiological variable. Table 4 reports instead a subset of coefficients representing the maximum instantaneous damage Δ and the maximum rate of worsening α, for several couples lesion-physiological variable (non-zero coefficients are relative to couples where the lesion produces damages on the corresponding variable).As already said, the patient dynamics is described by means of normalized physiological values.

Table 4: Instantaneous maximum damage Δ and maximum rate of worsening α

	B1 Delta	B1 Alpha	....	C2 Delta	C2 Alpha	....	D1 Delta	D1 Alpha	E Delta	E Alpha
Head/Neck	-0.3	-1.2	....	0	-0.6	....	-0.9	-1.2	-0.1	-0.3
Face	-0.2	-1.2	....	0	-0.6	....	-0.6	-0.6	-0.1	-0.3
Chest	-0.9	-0.6	....	-0.9	-1.2	....	-0.4	-0.6	-0.1	-0.3
Abdomen	-0.2	0	....	-0.9	-1.2	....	-0.2	0	-0.1	-0.3
Extremities	0	0	....	-0.5	-1.2	....	-0.2	0	-0.1	-0.3
External	0	0	....	-0.4	-0.6	....	0	0	-0.9	-0.6

3.2.2 Health care effect model (T3.2 Stadium Crush scenario)

The goal is the continuous assessment of the evolution of the patient health status with respect to the evolving time and in the presence of treatments administered, modeling the effect of treatment and first aid personnel activities in case of crisis.

The evolution is determined by the initial variable status (the initial defect), the initial rate of worsening and by the therapeutic maneuvers (if any) delivered. In the present formulation, medical care is delivered by structures, which for the purpose of the current project are called Health Care Facilities or Assets. A non-exhaustive list of possible assets is the following:

- Ambulance;
- Emergency Room;
- Operating Theatre;

- Police car;
- First responders;
- Advanced Medical Post;
- Triage Area;
- Intensive Care Unit (ICU);
- General Surgery;
- Cardio Surgery;
- Neuro Surgery (NCH);
- Emergency & Trauma Surgery;
- Drugs/Devices;
- Radiology;
- Radiology TC;
- Radiology ANGIO;
- General ward;
- Blood bank;
- Emergency Department.

Each facility is characterized by the set of therapies it can deliver:

- Oxygen;
- Intubation;
- Ambu bag;
- Saline infusion;
- Blood infusion;
- General surgery (emergency);
- Neuro surgery (emergency);
- Orthopedic surgery (emergency);
- Tourniquet;
- Cricothyrotomy;
- Thoracic tube;
- Mechanical ventilation;
- Pelvic binder;
- Cardiovascular surgery (emergency);
- Angioembolization.

The health care model (T3.2)is an extension of the patient model (T 3.1), taking additionally into account the effect of the health care. In the context of the PULSE Platform, this model interacts with the health care facilities model (T 3.3), dealing with the assessment and prediction of availability of resources, since a therapy can be administered at time t only if available at that time.

The mathematical Health care effect model follows the same approach as the Patient model (the evolution is also governed by sets of Ordinary Differential Equations, ODEs), with the difference that this model takes into account a collection of therapeutic maneuvers (e.g.oxygen, intubation, ambu bag, saline infusion, blood infusion) in a set of health care facilities (e.g. ambulance, emergency room, operating theatre, police car, first responders, advanced medical post).

In the normal form of first order, the evolution of each variable satisfies the following differential equation:

$$\frac{\mathrm{dx(t)}}{\mathrm{d}t} = -\alpha + u(t) \qquad t \geq t_0 \qquad (3)$$

starting from the initial condition:

$$x(t_0) = 1 - \Delta \qquad (4)$$

where:

- t_o is the start of the event;
- x(t) is the value assumed by each physiological variable at time $t \geq t_o$, when the damage of each variable starts. Each variable takes values in [0,1], where 1 is the initial healthy value, and has a lower-bound value under which the patient's health is compromised;
- $x(t_o)$ is the value assumed by each physiological variable at time $t = t_o$;
- dx(t)/dt = v(t) is the speed at which each variable changes its state;
- Δ: $\Delta \in [0,1]$ is the maximal initial increment at time t_o;
- α: $\alpha \in \mathbb{R}_o+$ is the maximal healing rate [relative healing/unit time];
- u(t) is a non-negative therapy component.

An asset set has been built, including (among others) ambulance, emergency room, operating theatre (with possible variants and specializations); each asset can provide a collection of therapeutic maneuvers, among those listed in the previous page. Table 5 reports a subset of associations among Health care assets/facilities and therapeutic maneuvers (which therapies can be delivered by each asset).

Table 5: Association between health care facilities and therapeutic maneuvers. If the cell at the intersection of facility i and therapy j contains 1 this means that the facility i can deliver the therapy j

Facilities/therapies	Oxygen	Intubation	Ambu bag	Saline infusion	Blood infusion
Ambulance	1	1	1	1	0
Emergency Room	1	1	1	1	1
Operating Theatre	1	1	1	1	1
Police car	0	0	0	0	0
First responders	0	1	1	1	0
Advanced Medical Post	1	1	1	1	0
….	….	….	….	….	….

Each maneuver has an associated instantaneous increment and a healing rate for each physiological variable: the patient functionalities show a sudden relative increment Δ; then their rate of variation is increased by a rate α. During the crisis, assets will have a spatial position and will be allocated to patients according to their injuries and to their individual severity. The values (Δ,α) depend on the particular treatment and are different for each physiological variable.

Table 6 reports some coefficients representing the effect of the therapies on the physiological variables in terms of modifications of the instantaneous damage and of the rate of worsening.According to the resource allocated for each patient, the evolution of the treated patient is determined.

Table 6: Effects of some therapies on the physiological variables in terms of instantaneous modifications (in fraction) and of variation of the rate of worsening (in fraction/hour)

	B1 Delta	B1 Alpha	….	C2 Delta	C2 Alpha	….	D1 Delta	D1 Alpha	E Delta	E Alpha
Oxygen	0	0.06	….	0	0	….	0	0.06	0	0
Intubation	1	60	….	0	0	….	0.1	0.3	0	0
Ambu bag	0.5	30	….	0	0	….	0.05	0.15	0	0

Saline infusion	0	0	….	0.2	6	….	0	0	0.2	3
Blood infusion	0	0	….	0.4	6	….	0	0	0.1	3
….	….	….	….	….	….	….	….	….	….	….

3.2.3 Health care facilities model (T3.3 Stadium and SARS scenarios)

In a Major Emergency, both the numbers affected and the health care requirements exceed the ability of the Health Services and Structures to provide adequate care on the basis of the resources available in "normal conditions". On top of that, the system resources are often quickly depleted during the evolution of the crisis. As a consequence, emergency management plans must be put into action to enhance the level of health care response; the knowledge of the capacity of the health services becomes a key point for decision support.
Several components of the PULSE platform will have to make decisions based on the availability of the health resources. One of the PULSE DSS components, which supports this decisional process phase, is the Health Care Facilities Model.

The final goal of this model in PULSE is to help in quantifying the imbalance among optimal care needs, resources availability and any on-going reductions in the levels of both.To this end,it considers the availability of resources for the following Hospital Types (HT) in case of Stadium Crush scenario:

- Trauma Center high level;
- Trauma Center low level;
- General Hospital;
- Specialized Hospital (Burns, Pediatric, Neuro, Cardio);
- First Aid (without beds).

For each category of hospital, it is possible to evaluate the availability (in unit of resource) of the following resources:

- Triage [pts/h];
- Emergency Room [number of beds];
- Intensive Care Unit (ICU) [number of beds/function];
- General Surgery [number of teams in house/on call];

- Cardio Surgery [number of teams in house];
- Neuro Surgery (NCH) [number of teams in house];
- Emergency & Trauma Surgery [number of teams in house];
- Drugs/Devices [% of the basal value];
- Ambulance [number];
- Radiology [basic/standard];
- Radiology TC [number];
- Radiology ANGIO [number];
- General ward [number of beds];
- OperatingTheater [number];
- Blood bank [level of function 1-5][1];
- Emergency Department[number treated pts/h].

In the case of SARS scenario, the considered Hospital Types (HT) are the following:

- Level 1 Infectious Disease (ID) Specialized Hospital;
- Level 2 Infectious Disease (ID) Specialized Hospital;
- Level 1 General Hospital;
- Level 2 General Hospital;
- General Practitioner Clinic.

For these categories of hospital, it is possible to evaluate the availability (in unit of resource) of the following resources:

- ID ward;
- High level isolation unit;
- ID specialist;
- General Practitioner;
- Infection control protocol for SARS;
- Treatment Protocol for SARS;
- ID specialist on call 7/24 (guard);
- ID specialist on call.

The following attributes need to be estimated for each resource of each HT:

- Basal level (L_0) [in resource units] (level in normal, non critical conditions);
- The time in hours(t_{50}) required to reach the 50% of the increment of the

[1] 5: 24 h, blood protocol, full functions; 4: 24 h, blood protocol, no full functions; 3: h 24, no blood protocol; 2: h12, on call; 1: on call.

resource with respect to the beginning of the crisis (t_0).

Table 7 reports an example of a subset of possible resources to be incremented to meet the needs during a Major Emergency in case of Stadium Crush scenario(levels are given for Trauma Center high level).

Table 7: Critical resources to be increased during a Major Emergency in case of Stadium Crush scenario

Resource name	Unit	Basal Level (L_0) [in resource units]	Time t_{50} [h]
Triage	pts/h	2	20
Emergency Room	number of beds	2	6
Intensive Care Unit (ICU)	number of beds/function	4	70
General Surgery	number of teams in house/on call	1	1
Cardio Surgery	number of teams in house	2	1
Neuro Surgery (NCH)	number of teams in house	2	1
Emergency & Trauma Surgery	number of teams in house	2	1
Drugs/Devices	% of the basal value	1	100
Ambulances	number	1	1
Radiology	basic/standard	0.5	1
Radiology TC	number	0.5	3
Radiology ANGIO	number	1	1
General ward	number of beds	5	200
Operating Theaters	number	0.5	2
Blood bank	function level 1-5	1	5
Emergency Department	number treated pts/h	2	10

Table 8 reports an example of a subset of possible resources to be incremented to meet the needs during a Major Emergency in case of SARS scenario(levels are given for Level 1 Infectious Disease (ID) Specialized Hospital):

Table 8: Critical resources to be increased during a Major Emergency in case of SARS scenario

Resource name	Unit	Basal Level (L_0) [in resource units]	Time t_{50} [h]
ID ward	number of beds	40	2
High level isolation unit	number of beds	2	n.a.
ID specialist	number	3	1
General Practitioner	number	n.a.	n.a.
Infection control protocol for SARS		n.a.	n.a.
Treatment Protocol for SARS		n.a.	n.a.
ID specialist on call 7/24 (guard)	number	1	2
ID specialist on call	number	1	2

For a desired prediction interval delta_t, the mathematical Health care facilities model returns the prediction of the amount of the resource R at time t+delta_t, given the availability of the nominal level $L_0$of the resource at time t. The evolution is governed by the Hill function (5) (Fig.1):

$$L(t + delta\_t) = L_0 + \Delta_{max} \frac{(t - t_0)^\gamma}{(t_{50} - t_0)^\gamma + (t - t_0)^\gamma} \qquad (5)$$

where:

- $\Delta_{max}= \Delta_{10}\log(num\_affected)$;
- $\Delta_{10}= L_0$;
- t_{50} is the time required to reach the 50% of the maximal increment of the

resource with respect to t_0, as a function of the hospital type (HT);

- γ affects the progressiveness in making new resources available (e.g. γ=2).

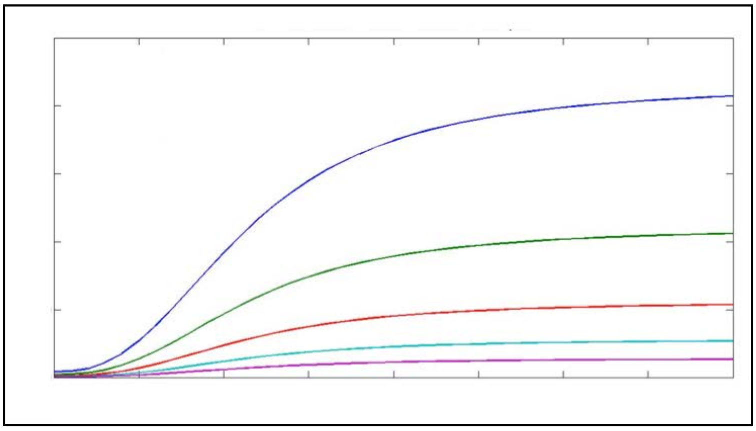

Figure 1: Examples of trend for Hill Function.

An illustration of the use of the model is given in Fig. 2. Note that forecast of the provision of the resource R depends on the number affected, according to the hospital policies which commonly increase the level of critical resources in order to meet the specific needs. Furthermore, different hospital types are able to provide different levels of surge capacity for the same resource given the same crisis conditions.

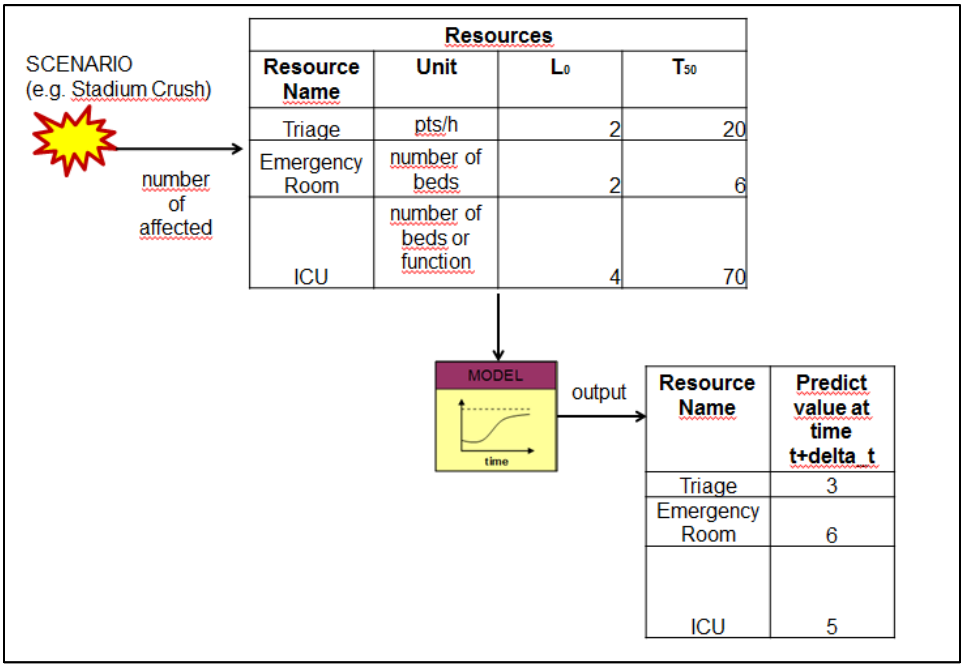

Figure 2: Architecture of the Health care facilities model.

3.2.4 Evolution model for biological events (T3.6 SARS scenario)

The goal of the Evolution model for biological events (ENSIR model) is the prediction of the spatial evolution of an epidemic.It takes into account geographic factors, allowing for disease spread with different rates depending on the social and logistic characteristics of the interested area. The main geographic and social factors taken into account are:

- the number/density of population in the interested area;
- the 'natural' connectivity of population, which may depend on the geography of the area;
- the connectivity by means of transportation, daily flights, etc.

ENSIR (ENhanced SIR) is an evolution of well-known SIR (Susceptible - Infected - Recovered) and SEIR models. In a SEIR model, each individual can assume one over 4 possible states, partitioning the individuals into 4 subpopulations:

1. Susceptibles S: members of the population who are susceptible to the infectious agent, not yet infected but they may become infected.

2. Exposed E: members of population infected by the SARS virus, in the incubation

period, asymptomatic, possibly infectious (without infectivity or with very low infectivity).

3. Infectious I: members of the population who are infected and infectious with strong infectivity.

4. Removed R: members of the population who have recovered from the disease with full immunity against reinfection, or members who died, or those that are either isolated or quarantined.

The model is based on nonlinear ordinary or delay differential equations. The differential equations of the SIR model (which does not consider the exposed population, i.e. the incubation period) are the following:

$$\frac{dS}{dt} = -K_{IS} * S * I$$

$$\frac{dI}{dt} = K_{IS} * S * I - K_{RI} * I$$

$$\frac{dR}{dt} = K_{RI} * I$$

The differential equations of the SEIR model are the following:

$$\frac{dS}{dt} = -K_{ES} * S * I$$

$$\frac{dE}{dt} = K_{ES} * S * I - K_{IE} * E$$

$$\frac{dI}{dt} = K_{IE} * E - K_{RI} * I$$

$$\frac{dR}{dt} = K_{RI} * I$$

where K_{XY} is the transfer rate from the state Y to the state X.

With respect to SEIR, ENSIR considers the values of the subpopulation (S_i, E_i, I_i, R_i) in each cell i, and determines the rates of variations of (S_i, E_i, I_i, R_i) in cell i as a function of the subpopulations (S_j, E_j, I_j, R_j) of each neighbouring cell j of i.

To this aim, it is possible to choose among three different types of neighbourhood function of cell i (NBD(i)):

1. Complete graph (Fig.3): all cells are neighbour of cell i, including the cell i;

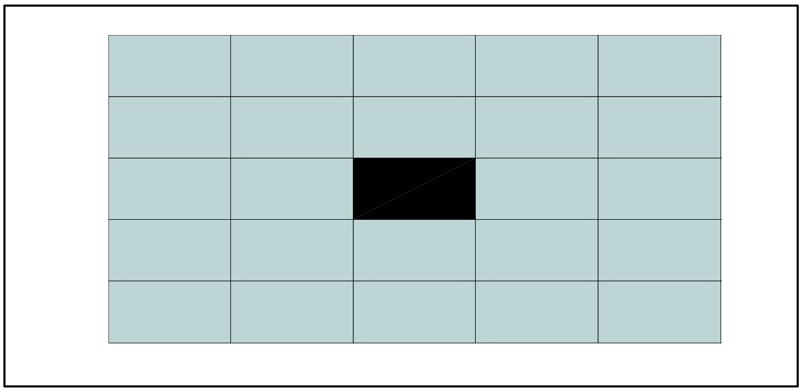

Figure 3: Complete graph.

2. Moore neighborhood (Fig.4): cell j is neighbour of cell i if $\max(|c_j - c_i|, |r_j - r_i|) \leq 1$, where r_i,$r_j$are the rowindices of cell i, j, and c_i,$c_j$are the column indices of cell i, j, respectively.

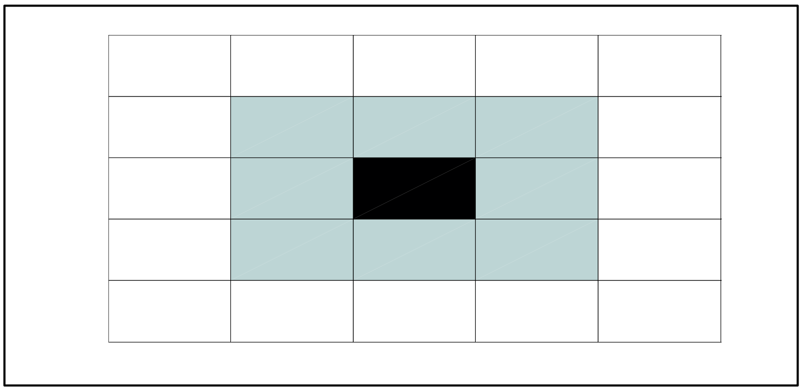

Figure 4: Moore neighborhood.

3. Von Neumann neighborhood (Fig.5): cell j is neighbour of cell i if:$|c_j - c_i| + |r_j - r_i| \leq 1$.

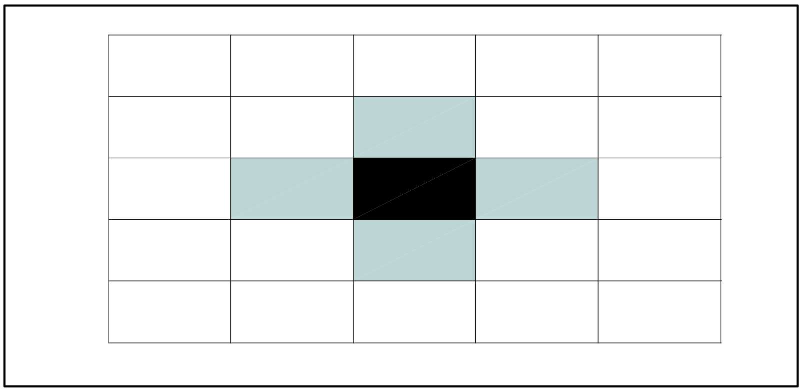

Figure 5: Von Neumann neighborhood.

As already mentioned, the evolution model for biological/epidemics events takes into account geographic, social and logistic factors of the relevant environment. An example is given in Fig. 6, where an area including northern and central Italy is considered and is partitioned according to a grid of dimensions [num_rows x num_columns], with num_rows=num_columns=20. The total number of cells num_cells =num_rows* num_columns is equal to 400.

In the ENSIR model, three matrices are allocated to manage the information regarding population and connectivity:

1. M_pop: Initial Population Matrix,with dimension [num_rows x num_columns], where each entry is an integer value counting the population of the corresponding cell.An example is provided in Fig.7, using different colors.

2. M_conn: Rate of 'natural' connectivity between cells, with dimension [num_cells x

num_cells], where each entry is a nonnegative real number;M_conn(i,j) is a function of the physical distance between the centres of cell i and cell j and of the populations of cells i and j. M_conn(i,i) is set equal to a strictly positive number to take into account the internal infectivity (within the same cell).

3. M_vol: Connectivity Matrix by the daily transportations (flights) between cells, dimension [num_cells x num_cells], each entry is a nonnegative integer.

The general connectivity matrix K is computed as K=M_conn+ r*M_vol, where r is a design parameter. The connectivities K_{ij}related to any pair (cell i, cell j) appear in the ENSIR equations as scaling factors, affecting the rate of spatial transmission of the epidemics between the corresponding cells.

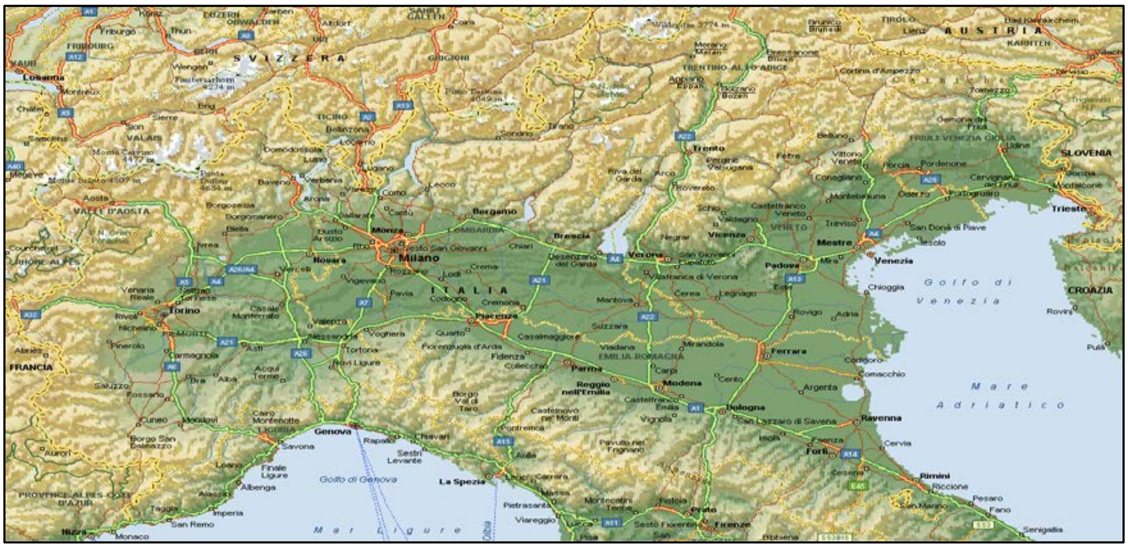

Figure 6: Example of interested area, Northern and Central Italy.

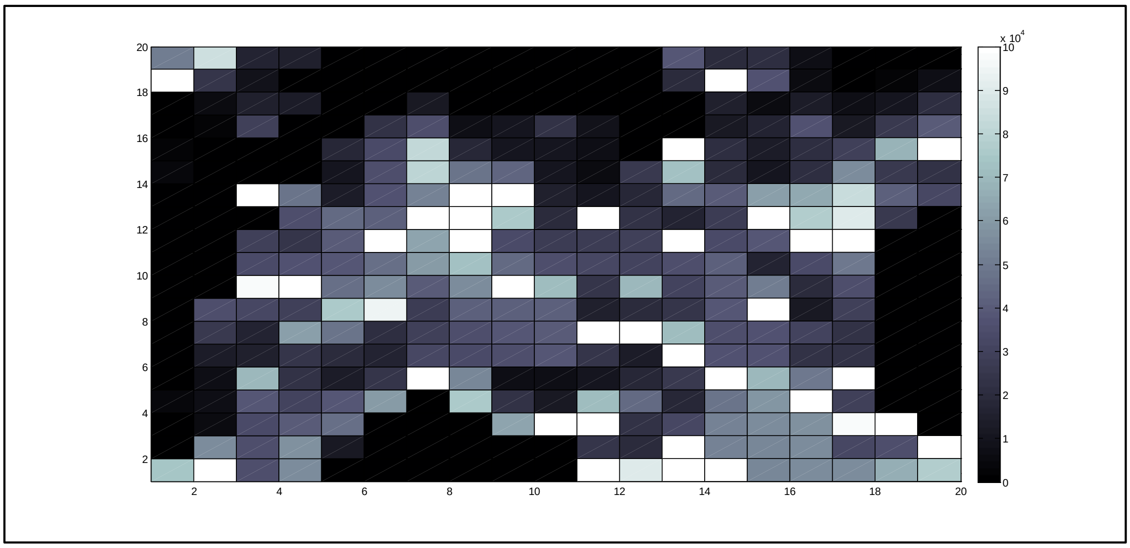

Figure 7: Example of Initial Population Matrix M_pop for Northern and Central Italy.

4 Architecture

In the overall PULSE architecture, the WP3 suite of models and algorithms provides the simulation engine for the WP4 tools, from which the models will be extensively called.

The models are accessible as webservices on the LAMP (Linux-Apache-MySQL-PHP) server located in the Biomathematics Laboratory of CNR-IASI at the UCSC Gemelli hospital,and constitute the core of the modeling prototypes. For the purpose of the present deliverable, a synthetic client in form of a Graphical User Interface (GUI) has been designed for testing the connection to the webservices and to perform basic tests on a subset of functionalities. The software technology underlying the general client-server architecture is better described in Section 5.

4.1 Server Architecture: model functions

The mathematical models described in the previous section are implemented on the server by means of "services", which can be conceptually considered as functions taking some arguments as inputs and returning a desired output.

4.1.1 Patient model function (T3.1 Stadium Crush scenario)

This function simulates the physiological evolution of a patient or a cohort of patients, if no therapy is administered. The number of patients considered is referred to as "num_affected", the constant number of physiological variables (equal to 10) is denoted by "num_variables".

<u>INPUT</u>

1. Physiological State $X_t$at time t, matrix dimension [num_affected x num_variables], each entry with value in [0,1].

2. PhysiologicalRate of changeV_t at time t, matrix dimension [num_affected x num_variables], each entry real-valued, [1/h].

3. Time stepdelta_t, nonnegative real number [h].

<u>OUTPUT</u>

1. Physiological State$X_{t+delta_t}$at time t+delta_t, matrix dimension [num_affected x num_variables], each entry with value in [0,1].

2. PhysiologicalRate of change $V_{t+delta\_t}$ at time t+delta_t,matrix dimension [num_affected x num_variables], each entry real-valued, [1/h].

4.1.2 Health care effect model function (T3.2 Stadium Crush scenario)

The function simulates the physiological evolution of a patient or a cohort of patients, when therapy is administered by means of health facilities (also called resources or assets). The number of patients considered is referred to as “num_affected”, the constant number of physiological variables (equal to 10) is denoted by “num_variables”. The health facilities are chosen within a set denoted by “asset_set”. Examples of asset sets have been given in the previous section.

INPUT

1. Physiological State X_t at time t, matrix dimension [num_affected x num_variables], each entry with value in [0,1].

2. Physiological Rate of change V_t at time t, matrix dimension [num_affected x num_variables], each entry real-valued, [1/h].

3. Applicable Asset vector asset_vec, vector dimension [num_affected], each entry with values in asset_set.

4. Prediction time stepdelta_t, nonnegative real number [h].

OUTPUT

1. Physiological State $X_{t+delta\_t}$ at time t+delta_t, matrix dimension [num_affected x num_variables], each entry with value in [0,1];

2. Physiological Rate of change $V_{t+delta\_t}$ at time t+delta_t, matrix dimension [num_affected x num_variables], each entry real-valued, [1/h].

4.1.3 Health care facilities model function (T3.3 Stadium and SARS scenario)

The function returns the prediction of the amount of a chosen resource R (chosen in the set asset_set), at time t+delta_t, given the number “num_affected” of the people involved in the crisis scenario, the type HT of the hospital (chosen in the set category_set), the level L_0 of the resource at time t. The sets category_set and asset_set depend on the scenario. Examples have been given in Section 3.

INPUT

1. Number of affectednum_affected, natural number.

2. Hospital Type HT, with values in category_set.

3. Resource name/identifierR, with values in asset_set.

4. Resource levelL_t at time t, in unit of the resource.

5. Prediction time stepdelta_t, nonnegative real number [unit of time].

OUTPUT

1. Prediction$L_{t+delta_t}$ of the provision of resource R at time t+delta_t.

4.1.4 ENSIR model function (T3.6 SARS scenario)

Given a time horizon T and a sampling time delta_t, the function computes the expected evolution of the epidemics, starting from a spatial initial distribution of exposed (E_start) and infected (I_start) individuals within n_e and n_i cells of the grid, respectively.The dimension of the grid is [num_rows x num_columns]. The event type corresponds to the SARS epidemics. Given a number num_assets of possible resource types (e.g. specialized hospitals) to allocate for the treatment, in the vector asset_vec it is possible to specify the availability of each resource type. The number of time samples obtained in the interval (0:T) with time step delta_t is denoted by length_T. The function returns the temporal evolution of the cumulative subpopulations (i.e. summed over all the cells of the grid) of Susceptibles, Exposed, Infectious, Recovered (vectors of dimension equal to length_T), along with the evolution of the total count of infected people.

INPUT

1. Exposed Matrix E_start: matrix dimension [n_e x 3], with each row containing

[cell row_index, cell column_index, number of exposed in the cell at initial time].

2. Infected Matrix I_start:matrix dimension [n_i x 3], with each row containing

[cell row_index, cell column_index, number of infected in the cell at initial time].

3. Asset vectorasset_vec,vector dimension [num_assets],each entry nonnegative integer.

4. Time horizon (T), nonnegative real number.

5. Time step delta_t, nonnegative real number.

6. Event typeevent_type (default: SARS).

OUTPUT

1. Evolution of the subpopulation counts[S, E, I, R], matrix dimension [length_T x 4].

2. Evolution of the infected subpopulationI_tot, vector dimension [length_T].

4.1.5 Additional services

The described models (in particular those pertaining to tasks T3.1 and T3.2) contemplate some related functions:

1. Simple Triage: from the physiological states and the worsening rates at time t, it returns the triage color code(i.e. black, red, yellow, green) for a cohort of patients.

2. ETD: from the physiological states and the worsening rates at time t, it returns the Expected Time to Death (ETD) for a cohort of patients.

3. Sympter: the values of physiological states and worsening rates determine the occurrence of compatible symptoms, sampled according to a probability distribution(see Table 9for the symptoms descriptions). This enables having a global vision of the status of the affected people and to train and test the performance of the personnel in the triage procedure, which is performed from the detected symptoms.

Table 9: Examples of compatibility between symptoms and a damage in a particular physiological dimension (1=compatibility)

SYMPTOM DESCRIPTION	….	B1	….	C1	….	D3	E
Apnea with open airway	….	1	….	1	….		
Tachypnea	….	1	….		….	1	
Bradypnea	….	1	….		….	1	
Eupnea	….	1	….		….		
CR (>2sec)	….		….	1	….	1	
CR (<2sec)	….		….	1	….	1	

Alert	….	1	….	1	….		
Responsive to Voice	….	1	….	1	….		
Response to Pain	….	1	….	1	….		
Unresponsive	….	1	….	1	….	1	
Cannot walk	….	1	….	1	….	1	
Can walk	….	1	….	1	….		
….	….	….	….	….	….	….	….

4.2 Client Architecture: GUI description

The client consists of a Graphical User Interface (GUI) calling the models running on the CNR-IASI at the UCSC Gemelli hospital.

The GUI presents an interface with 3 tabbed panes (see Fig. 8, 9,10). In the following, if not specified otherwise, the inputs which are not selectable from the graphical interface are set to default values.

- The first tabbed pane (Fig.8) is a basic test covering T3.1 and T3.2. One can choose the values of the physiological state and their rates of change for a patient. It is possible to perform a triage based on the physiological state. Then, the evolution of the patient within a selectable time horizon can be retrieved, in absence of health care and in the presence of a therapy, which can be chosen from a list of possible treatments. The updated triage color at the end of the considered time horizon is also shown.
- The second tabbed pane (Fig.9) is a basic test of the Health Care Facilities Model (T3.3), for a list of facilities (at the moment, limited to the Stadium Crush Scenario). It is possible to choose the facility, the hospital type and the time horizon for the prediction. The predicted value (in the presence of surge capacity) is returned. A refined test of the Health Care Facilities Model will be performed by means of the Logistic Tool in WP4.
- The third tabbed pane (Fig.10) is a basic test of the evolution model for biological events (T3.6), for the SARS scenario. It is possible to choose a time horizon and an initial number of infected and exposed people, which are

inserted into a chosen cell of the grid. The client calls the corresponding webservice and some textual results are shown, as the total number of infected and the maximum number of exposed during the epidemics. A refined test of the evolution model for biological events will be performed by means of the ENSIR Tool in WP4. Figures 11 and12 show some sample plots of a possible epidemics evolution (obtained by means of an external client with data returned by the webservice).

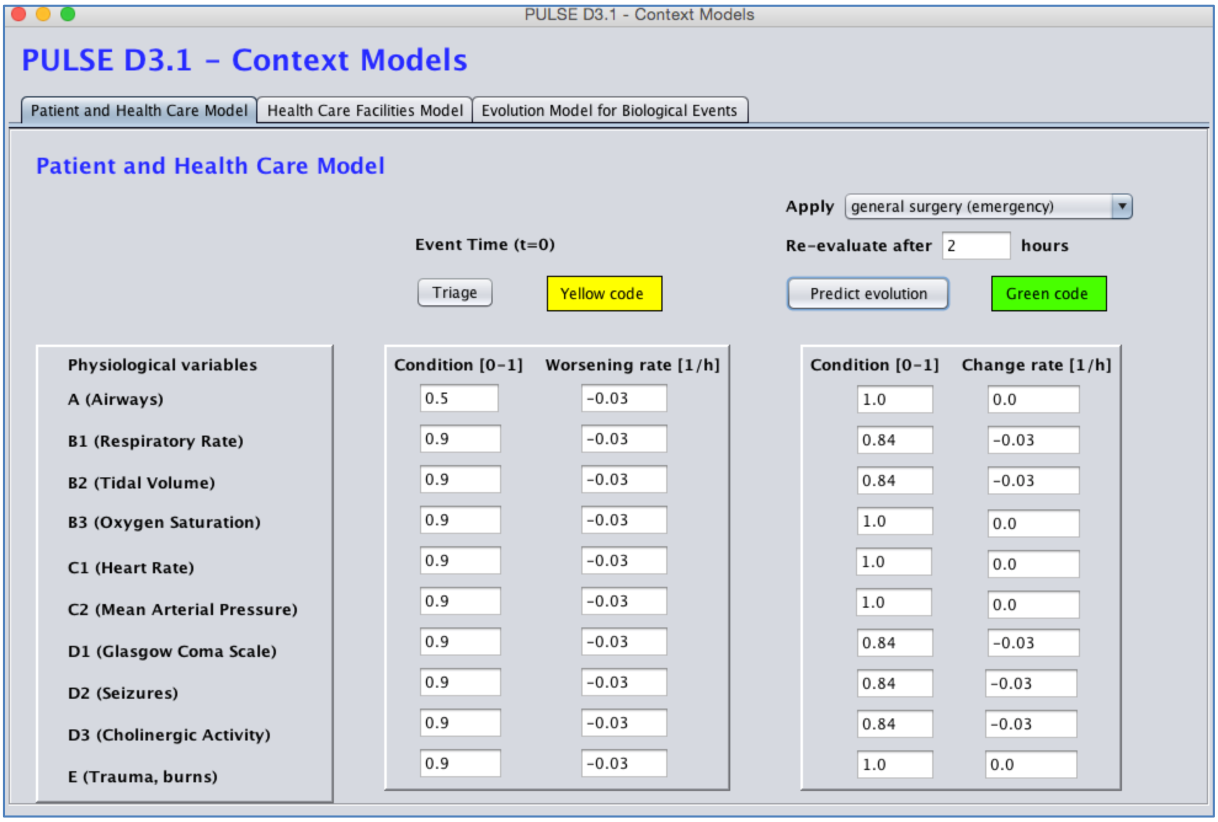

Figure 8: Client prototype - Patient and Health care Model

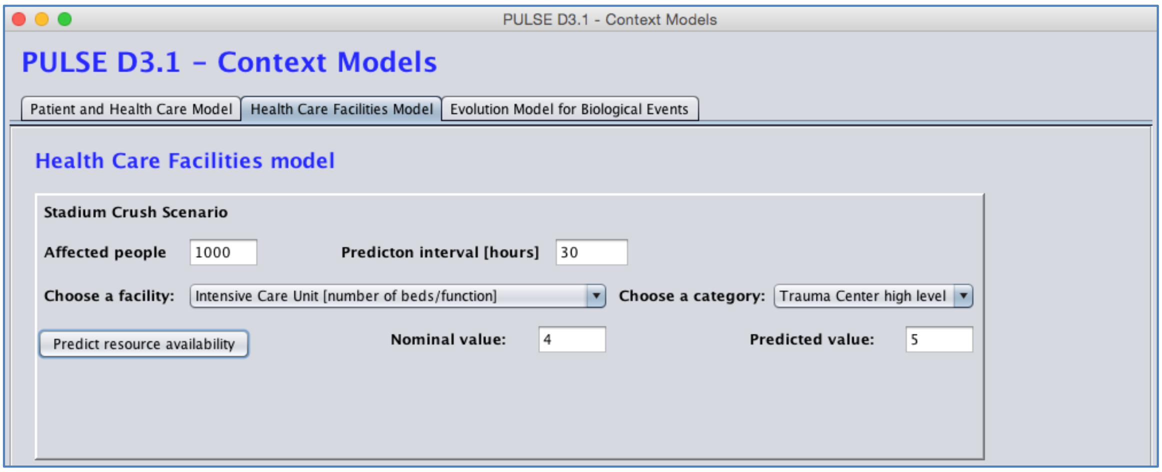

Figure 9: Client prototype - Health Care Facilities Model

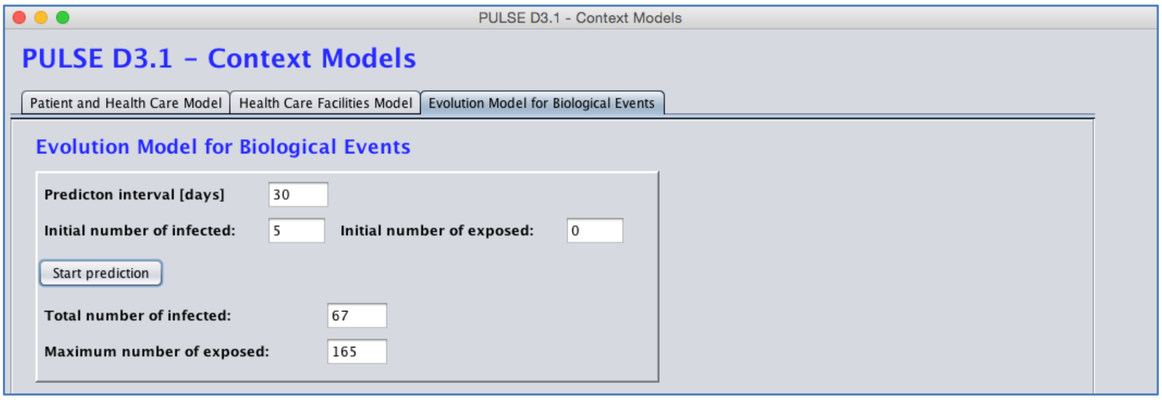

Figure 10: Client prototype - Evolution Model for Biological Events

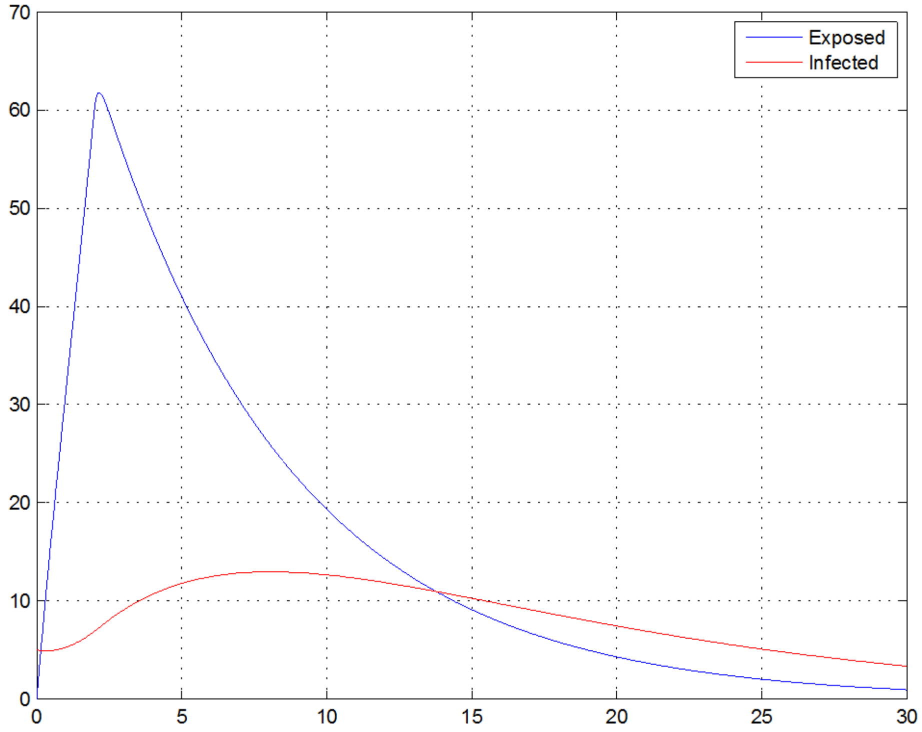

Figure11: Trends of Exposed and Infected population within a time horizon of 30 days in a possible epidemics evolution.

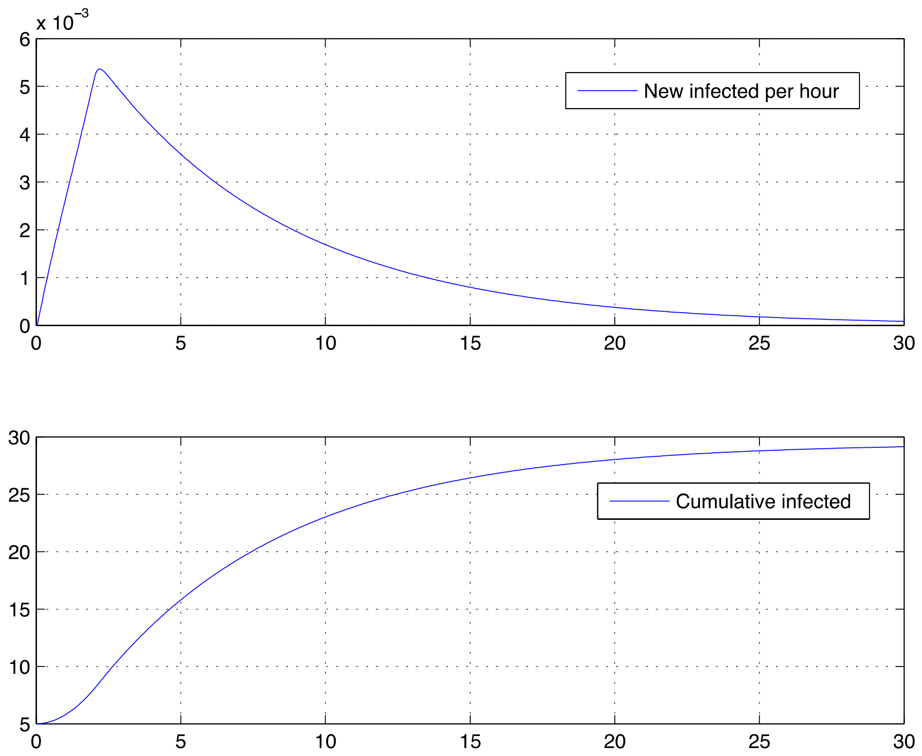

Figure 12: Rate of infection (top panel) and cumulative infected population (bottom panel) within a time horizon of 30 days in a possible epidemics evolution

5 Underlying Technologies

5.1 Core technologies

As already mentioned in the description of the architecture, the models described in the previous sections are implemented by means of webservices. The architecture at the basis of a webservice is formed by a *server* and one or more *clients*. The client is able to know the functionalities offered by a server by means of the *Web Services Description Language* file (wsdl), which is located at the web address:http://biomat1.iasi.cnr.it/webservices/pulse/M14/webservice.wsdl.

The webservices are implemented in php language, and communicate with the clients according to the SOAP protocol, which provides a basic messaging framework for web services. In such a way, the client is able to send requests even in another programming language (i.e. Java) with respect to the server, though respecting the SOAP specifications. Both the requests and the response are exchanged in XML language (Fig.13).

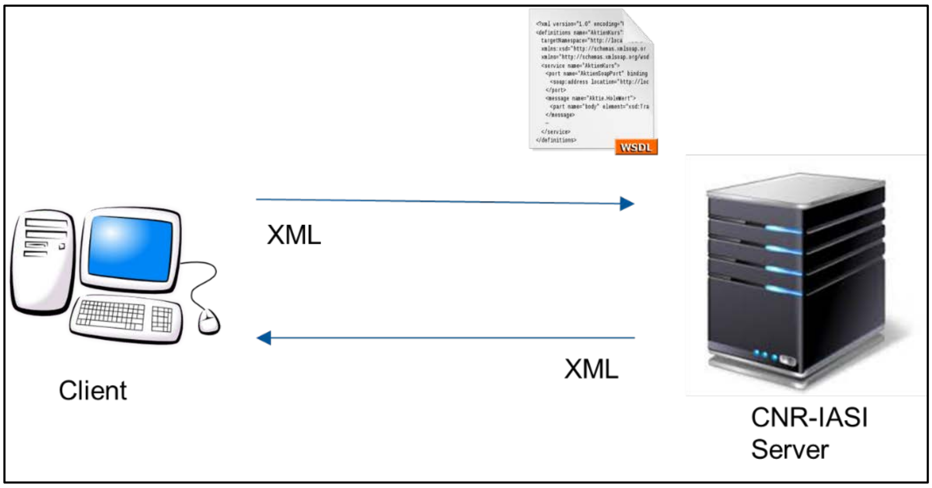

Figure 13: Scheme of the architecture used for the service.

On the client side, a synthetic Graphical User Interface (GUI) has been designed for testing the connection to the webservices and to perform basic tests on a subset of functionalities. The GUI has been implemented in the Java programming language by means of the Swing componentsin Oracle's Netbeans IDE.The prototype is distributed in the form of Java Archive (.jar) and is executable on any computer with a Java Virtual Machine (JVM) installed on it, by typing

```
java -jar "PULSE_D31.jar"
```

from the command line, after entering the folder containing the java archive.

Internet connection is required for the client to allow the access to the model web services and the correct retrieval of the results.

5.2 3rd Party libraries and licenses

Below is a list of third party libraries/frameworks used and the licenses under which they are distributed.

Table 10: 3rd party libraries and licenses

Product	Version	Vendor	License
Java SE Development Kit	8	Oracle	Oracle Binary Code License Agreement
Beans Binding	1.2.1	Java.net	GNU LESSER GENERAL PUBLIC LICENSE
Swing Layout Extensions	1.0.4	Java.net	GNU LESSER GENERAL PUBLIC LICENSE

6 Software Test/Validation and Relation to other Deliverables/WPs

The client which is the object of the present deliverable has been designed to test the basic functionalities of the model implementations of the server. As shown in the previous sections, the model webservices are called with a subsets of input choosable by the user, while some other inputs are fixed.

Parameter tuning and implementation refinements are the object of future deliverables in the second half of the project. Within WP3, the deliverable D3.2 “Scenario Generation” (due at M18) will allow for an integrated simulation of the two scenarios (extensively described in the WP2 deliverables), where the model functions (now called separately) will be jointly fed by inputs provided by the Scenario Generator. The M18 version of the model functions may also include refinements and take into account procedures from the cuncurrent WP5 deliverables.

Furthermore, with respect to the design of the WP4 tools, the Health Care Facilities Model and the Evolution Model for Biological Events will constitute the basic modeling layer of the prototype deliverables D4.4 (Surge Capacity Tool) and D4.7 (ENSIR), respectively, due at M18. Within these deliverables, refined prototypes will be issued, allowing the placement of a larger set of parameters and the retrieval of some results in a graphical form. In the final year of the project (M19-M30), the processes of integration and validation/trials in WP6-WP7 will provide further occasion for tuning the model parameters as a consequence of the lessons learnt and of the application of the PULSE platform in realistic conditions for the considered scenarios.