PYOCYANIC BACILLUS PROPAGATION SIMULATION

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ABSTRACT

Nosocomial diseases are pathologies that appear during medical care that were not present at patient admission. Being able to simulate the propagation of such diseases inside an hospital and to track them is therefore important to fight and avoid them. The Pyocyanic Bacillus is a frequent example of such a disease. It is important to understand how such bacteria propagate since more and more of their strains become antibiotic resistant. Therefore we must not only be able to treat them, but also to block their diffusion to avoid them. The work presented here consist in a simulation of the propagation of pyos inside an hospital taking spatial problems into account, and allowing to better understand the infection diffusion mechanisms and to propose some means to circumvent it. The simulation considers both the spacial representation of the hospital, and the different actors, healthcare workers, patients and visitors.

KEYWORDS

Pyocyanic bacillus, Antibiotic, Nosocomial, IBM, ACO, Ant Algorithm.

INTRODUCTION

Pyocyanic Bacillus (Pyo) or Pseudomonas Aeruginosa (Figure 1) is a pathogen bacteria that is often found in eye, lung, or bladder infection and wound or burn infection for example. Pyos generate the pyogenic process, that is, pus formation. Indeed, bacterias multiply on the infection site, causing the massive production of neutrophils that phagocytose bacterias. These neutrophils die therefore producing pus.

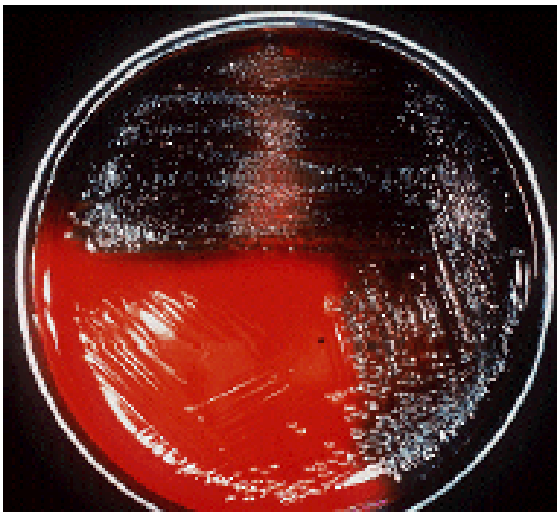

Figure 1: Pyocyanic Bacillus Colony.

Pyos are one of the most often encountered nosocomial disease. They are easily communicated by contact between patients and healthcare workers. Furthermore, Pseudomonas Aeruginosa is a bacteria that is naturally resitant to antibiotics and quickly adapt to medicine treatments. When antibiotic treatments have already been administered, this bacteria becomes particularly resistant, which is the case in hospitals. If such strains persist in an hospital they can severely complicate patient treatment.

In [2], Helen Giamarellou says that: “Almost 50 years ago, Pseudomonas aeruginosa was rarely considered as a real pathogen [...] the emerging resistance problem of Pseudomonas will worsen while the approaching era of ’the end of the antipseudomonal

antibiotics' will become a nosocomial nightmare.

Therefore, not only we must search means to treat it, but it is necessary to block its proliferation and communication ways.

We propose a simulation of the infection propagation using a model representing spatially an hospital, and using a concrete representation of individuals. Such a model is called an individual based model (IBM). This simulation should help us to track the infection diffusion and to discover its mechanisms, for example infection reservoirs, or the common passage points for the infection.

The model should then be used to both visualize the infection path from already collected data, and to simulate an hypothetical infection. With such a model, it is possible to develop algorithms that can detect infections paths and areas inside the hospital. Further this model could be used to devise a analytical and deterministic model whose trajectory study would be easier.

The next section details the model, and take as example the Jacques Monod Hospital from which series of data on the Pyocyanic Bacillus has been collected. In the following section, the simulation of an infection is described and preliminary results are presented. Finally, an algorithm allowing the detection of infected areas using the ant metaphor is discussed.

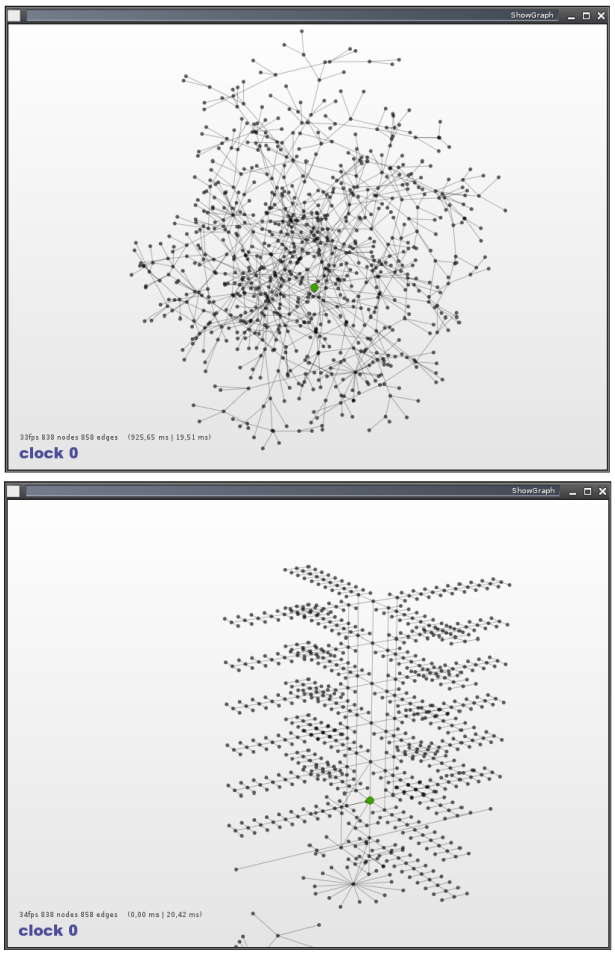

Figure 2: Two visualizations of the graphs representing the hospital Jacques Monod.

MODEL AND VISUALIZATION

The model focuses on a spacial representation of the hospital and, for the simulation, of individuals. We can distinguish at least two important classes of individuals : employees and patients. These classes can then be subdivided into sub-classes, for example doctors and nurses for employees.

To define a common spacial representation that could fit almost any kind of hospital, the building is represented as an undirected graph $G = (V, E)$ with V the set of vertices and E the set of edges. Vertices of the graph represent distinct sectors in the hospital, patient rooms, waiting-room, operating-room, etc. Edges of the graph represent paths between these sectors. The figure 2 shows the Jacques Monod hospital using this representation. On top the graph representing the hospital, under, the same graph but constrained by the physical layout of the building. This construction is arranged as a cross, making it easy to put a wing in quarantine, but also forcing the employees and visitors to use very common passage points.

Individuals move inside the graph from vertex to vertex following the edges, and interact one with another. Individuals have a path inside the graph. These path can be of two forms, they can be:

- predefined, if we are replaying data provided by an hospital;
- programmed, if we are simulating an infection.

For predefined paths, collected data often contains only series of locations or merely the starting sector and end sector. In this case the simulator is able to reconstruct a path following constraints. Often a A^* or Dijkstra algorithm are used to recreate the path. However using such algorithms can lead to different results since patient and healthcare worker displacements are often not optimized this way. Individuals can wait on each node, and cross edges at a given speed.

SIMULATION

Records of displacement and infection status of each patient, are not easy to maintain. Often only the medical state of the patient is recorded, not its movements. Furthermore as we are interested in nosocomial diseases, it would be interesting to process data concerning healthcare workers, in addition to patients. Indeed, in nosocomial diseases, the hospital plays the role of reservoir of resitant bacterias, and it is the employees that propagate the infection.

In addition, we do not know which sectors of the hospital may eventually become reservoirs for antibiotic resistant bacteria strains. That is, in our model, we often do not know if a vertex is infected or not.

To accommodate the miss of data, the model can be simulated, that is individuals behavior can predefined instead of merely reading and interpolating data. Patients and healthcare workers will therefore move inside the hospital going from a starting point to a destination point using routes inside the graph. The way the routes are defined, and how starting and ending points are chosen can be changed.

To define how the infection propagates, an infected individual can infect another by contact. The model allows to specify the contact duration for the contamination to occur. Identically, sectors can be contaminated by individuals if they stay a given amount of time.

As said above, there exist at least two kinds of individuals, patients and healthcare workers. To define how the infection develop, we follow the model developed in [1]. In this model, healthcare workers are considered as carrying the infection: they are contaminated by patients and then are able to contaminate other patients. There will therefore be two states for individuals: contaminated and healthy. We also consider two bacteria strains. One is antibiotic resistant, whereas the other does not. When an individual is contaminated he will therefore also contain information about the kind of bacteria he carries.

The bacteria population for each patient evolves according to the following rules that can take into account an antibiotic treatment:

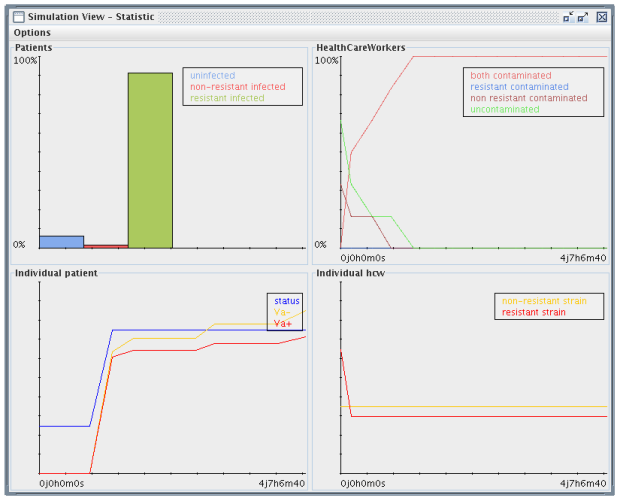

Figure 3: Statistic view of the simulator.

$$\begin{cases} \dfrac{dV^-(a)}{da} &= \left(-\dfrac{\tau V^+(a)}{V^-(a)+V^+(a)} \right. \\ &+ \left. \beta^-(a) - \dfrac{V^-(a)+V^+(a)}{\kappa_F}\right) \\ &\cdot \; V^-(a) + \gamma V^+(a) \\ \dfrac{dV^+(a)}{da} &= \left(\dfrac{\tau V^-(a)}{V^-(a)+V^+(a)} \right. \\ &+ \left. \beta^+(a) - \dfrac{V^-(a)+V^+(a)}{\kappa_F} - \gamma\right) \\ &\cdot \; V^+(a) \end{cases}$$

Where $V^-(a)$ is the non-resistant bacteria concentration at age a and $V^+(a)$ the resistant bacteria concentration. β^-, β^+, K_F, τ and γ are parameters allowing to regulate the bacteria population evolution.

Vertices of the graph can also be of several types. Normal vertices are non contaminated at start and can be infected if contaminated individuals cross or stay on them. Some vertices are considered as sterile and cannot be contaminated. To allow simulations, some vertices can also become contamination reservoirs, that is vertices that are always contaminated.

In addition to the visual representation of the hospital graph, the simulator allows us to follow the development of the infection during the simulation, as shown on figure 3.

USING AN ANT SYSTEM TO DETECT INFECTION AREAS

Given the simulation or replay of an infection using our model, we then search to detect infection paths as well as possible contamination reservoirs. That is, we search sectors where resistants strains of bacteria remain and can contaminate both healthcare workers and patients.

This problem is made more difficult since most of the time the patient infection is not detected as soon as it really occurs. Therefore, not only we have to consider the patient displacements when infected but also before his infection.

We propose to use the ant metaphor to detect the infection paths and reservoirs. The ant metaphor use numerical ants "travelling in the graph". The inspiration comes from the observation that real ants are able to detect the better path from their nest to a food source by dropping pheromones on the ground [3]. Pheromones are olfactory messages that attract other ants. The more of pheromones the more ants are attracted. Indeed, ants having found a good path whatever be the criterion for good, quicker, smarter, easier, will tend to deposit more pheromones on it. This can be implicit, for example shorter path are more quickly full of pheromones, or explicit, for example the ant detects the better path and choose to deposit pheromones on it.

Ants continuously travel in the graph and are continuously able to drop pheromones. An ant travels from vertex to vertex, choosing the next vertex in a balanced random way. That is, the ant chooses the next vertex according to some importance criterion that weight how many chances it has to choose it. In presence of pheromones, ants tend to choose the vertex that have more pheromones, but other criterions may be incorporated in this choice.

Such a behavior leads to more an more ants using important vertices and dropping pheromones on them, without neglecting other vertices, since they only have a larger chance to choose the important ones. Quickly, more and more pheromones are present on important vertices, therefore selecting them. This process increases with time, however pheromones evaporate which tends to avoid over increasing of pheromones values on largely used vertices, and avoid to select unimportant vertex after a long period.

Lets first give a broad idea of our method, inspired by [3] and [4]. In our model we can consider two types of "ants". The first one are the individuals inside the hospital. At the contrary of the ant metaphor they do not use information deposited in the graph to choose where to go. However they deposit information in the graph: infected vertices. The second type of ants we propose to add are numerical ants that try to detect infected vertices and paths, that we will call markers.

These later ants will be used at the end of an infection simulation or replay. Their goal is to find paths of infection. For this each ant randomly chooses a entering and destination point, and then explore the graph starting at the entering point, and visiting vertices until it reaches its destination. Each time a marker ant visits a vertex, it memorises it and chooses another vertex. A vertex memory allows to store the path used by the ant, and also to avoid to come back on an already visited vertex. That is, vertex in the ant memory will be avoided unless there is no other possible way (dead-ends for example).

The ant marker algorithm is iterative, at each time step t:

1. all ants move from their source to destination point, this is the "ant-tour";
2. ant paths are evaluated and selected.

The ant-tour process is also iterative. During one time step t of the algorithm, the ant-tour iterate all ants. At each of these ant-tour iterations, ants move from the vertex they are on to another vertex. The ant-tour is iterated until all ants reach their destination. As in the inspiring model, ants will choose the next vertex to visit in a balanced random way, according more chances to be chosen to vertices that are more infected and have more pheromones.

At the end of this displacement process, all ants paths are evaluated. Paths are sorted according to the number and value of infected vertices. Paths whose infection value is lower than threshold ψ are not changed, other paths edges are modified by dropping pheromones on them. This mimic the behavior of natural ants returning to the nest and dropping pheromones to indicate a good path.

This doubly iterative process is repeated until only a limited given number of paths pass the ψ threshold. At this time, the selected paths are considered as infection vectors.

Now we give the details of the method. The set of ants F at each ant-tour is constant. Ants drop

pheromones not on vertices bu on edges. This allows to select paths and not only vertices. The pheromone value on an edge (u, v) at time t is:

$$\tau^{(t)}(u, v)$$

Furthermore, at each time step, after the ant-tour, pheromone is added on edges according to ant paths. For an ant x the path is noted W_x and W is the set of all ants paths. The quantity of pheromone dropped by ant x on edge (u, v) at time t is noted:

$$\Delta_x^{(t)}(u, v)$$

and the sum of pheromones dropped by all ants on edge (u, v) at time t is:

$$\Delta^{(t)}(u, v) = \sum_{x \in F} \Delta^{(t)}(u, v)$$

At each time step t, pheromones evaporate. The quantity of pheromones remaining on edge (u, v) is:

$$\tau^{(t)}(u, v) = \rho\tau^{(t-1)}(u, v) + \Delta_x^{(t)}(u, v)$$

With $\rho \in]0, 1]$ the pheromone conservation factor.

The probability for an ant on vertex u to cross edge (u, v) choosing vertex v as its next position over all accessible vertices V_u is influenced by the quantity of pheromone on edge (u, v) and the infection value $w^{(t)}(v)$ of vertex v at time t for ant x:

$$\begin{cases} p_x^{(t)}(u, v) = \dfrac{\left(w^{(t)}(v)\right)^{\beta}}{\sum_{i \in V_u} \left(w^{(t)}(i)\right)^{\beta}} \\ \text{if } t = 0 \\ p_x^{(t)}(u, v) = \dfrac{\left(\tau^{(t)}(u, v)\right)^{\alpha} \left(w^{(t)}(v)\right)^{\beta} \eta_x(u)}{\sum_{i \in V_u} \left(\tau^{(t)}(u, i)\right)^{\alpha} \left(w^{(t)}(i)\right)^{\beta} \eta_x(i)} \\ \text{if } t \neq 0 \end{cases}$$

Parameters α and β are used to balance the relative importance of pheromones over the vertex infection. The factor $\eta_x(u)$ allows the ant to minimize the importance of vertices already visited. Indeed, for ant x considering vertex u:

$$\eta_x(u) = \begin{cases} 1 & \text{if} \quad u \in W_x \\ \eta & \text{if} \quad u \notin W_x \end{cases}$$

With $\eta \in]0, 1]$ allowing to minimize the importance of the vertex if it is already in memory $W_x \in W$ of ant x. When the ant-tour finished, the paths W are evaluated. The quantity $\Delta_x^{(t)}$ deposited by ant x on all the edges of its path is:

$$\Delta_x^{(t)} = \frac{W_x}{\max(W)}$$

The paths selected by ants show probable infection paths, but we are also interested at finding possible contamination reservoirs. The method we propose in order to do this, is to superimpose all found paths and detect common vertices. The importance of a vertex as a possible contamination reservoir is then the number of contamination paths crossing it.

CONCLUSION

In this paper a model has been developed that simulates the propagation of infections inside an hospital. The model is individual-based, and allows both the replay of data collected in hospitals, as well as the simulation of an infection propagation. The simulation allows to take into account data that was not or cannot be recorded in real situations. In addition to this model and simulation tool, a method to find infections path and contamination reservoirs inside the hospital that use the ant metaphor has been proposed. The hope of this work is to allow a better understanding of infection propagation and to propose means to stop it and also stop the continuous development of resistant bacteria strains.

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