Legionellosis pneumophila bacterium Developmental factors and their impact

Sacha Duperret

sduperret@u-bordeaux.fr
University of Bordeaux,
Simulating Life research team,
Talence,
France

March 9, 2022

Contents

List of Figures

Abbreviations

USA United States of America
L. pneumophila Legionella Pneumophila

Abstract

All the work in this document has been developed in the context of the simulating life teaching unit. This work will focus on the development of the legionellosis disease, and more particularly on the development of the bacterium which is the main cause, Legionella Pneumophila.The plan of this work is to evaluate in a computerized way and with a standardized methodology the accuracy of the current knowledge on the legionella pneumophila bacterium by reproducing experiments already performed in a controlled environment. The thesis is composed of three parts: the first part is intended to collect the latest knowledge on the l. pneumophila bacterium, as well as to format the data. The second part of the thesis corresponds to the setting up of the technical environment as well as the discussion of the technical solutions implemented. The third part is related to the simulation of the l. pneumophila bacterium under conditions of experiments already carried out in laboratory, whose characteristics were recovered and integrated in the simulation creates part two.

In chapter 1, I present the current knowledge on the legionella pneumophila bacterium and more particularly its development in a controlled environment. The simulation framework will be be covered in chapter 2, with a focus on the technical solutions found to face the problems of simulation of biological phenomena.

More than 10 experiments have been reproduced, which is important to verify that the program works correctly. This will allow in the future to implement additional experiments in a biology laboratory setting but also in the framework of our simulation, which will allow in fine to correlate the obtained data.

Bacteria details Legionella pneumophila is a ubiquitous bacterium, which colonizes artificial environments, wet soils as well as natural fresh water [1].

Bacteria transmission Bacteria are transmitted to humans by aerosolization and less often by aspiration (to the lung) of colonized water. For now, relation between infection and water ingestion (to digestive organs) is not demonstrated.

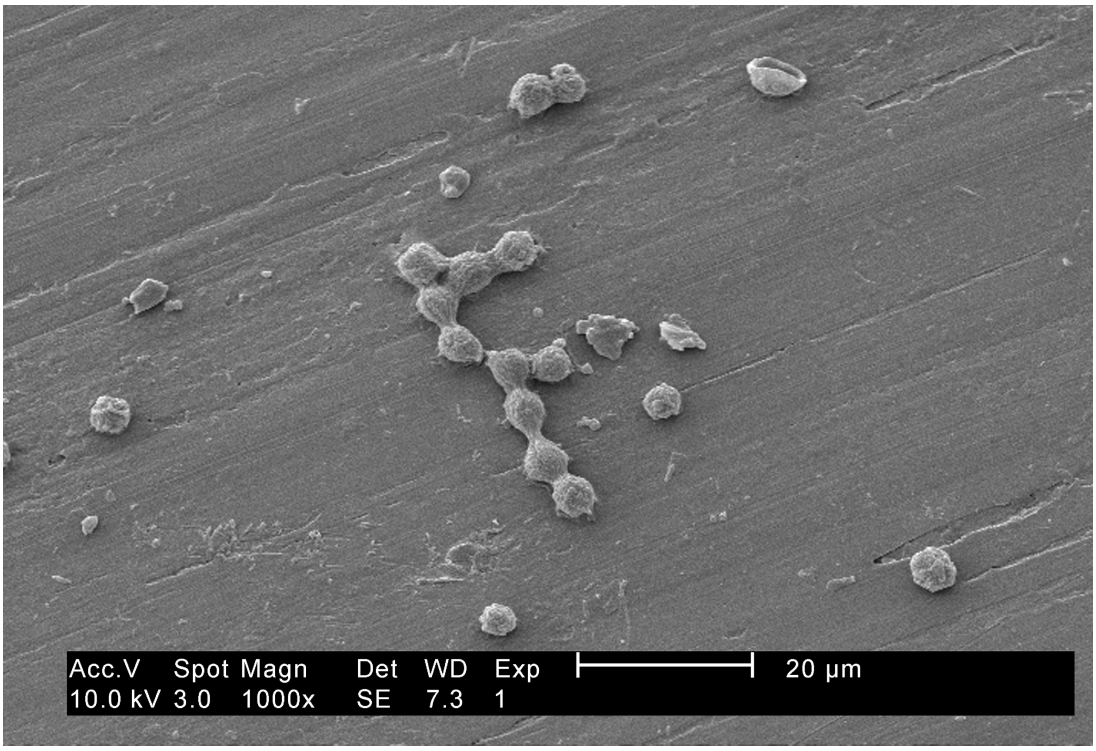


Figure 1: Legionella pneumophila bacteria (microscopy image)
Photo by Janice Haney Carr, Dr. Rodney Donlan, USCDCP

1 Introduction

1.1 Background

This research is conduct in parallel with the Simulating Life course, at the University of Bordeaux, Talence, France. The study goals is about L. pneumophila growing. Indeed this bacteria has an ability to cause Legionellosis disease.

1.2 Objectives

The objective is to consolidate the current data on these bacteria by testing them in a mathematical/computer simulation. This study is simulating various factor (for now only including basic bacteria colony growing $\Rightarrow$ in the future the objective is to add characteristics $\in$ temperature, water flow, pression, ... with effect on the bacteria[1] colony.

1.3 Methods

We started by simulating a bacteria colony growing normally and then added some characteristics with logic blocks which make explicit all the rules for the colony to grow (e.g. the bacteria can only

[1]Bacteria is plurial of bacterium

grow between certain temperature). *The intresting thing is that bacteria can develop without all the specific needs to be filled*

1.4 Results

After simulating a lot of randomized situation with the slnova.org©, we can see a statistical trend for the colony to grow much more with certain characteristics between limits. **What is interesting is that the scientific data acquired and validated by the community are analyzed in accordance with and logical for the organism studied in the context of the simulation.**

Figure 2: slnova.org logo (MIT)
From StarLogo Nova, it is a project of the MIT Scheller Teacher Education Program

1.5 Discussion

Many research team are currently working on legionella pneumophila bacterium and all the caracteristics we discuss on this report. The scientific bases and datas used may evolute. For update you can found the public (Licensed CC BY-NC-SA 4.0) project of this study, fork and update him. The result of the study can be discussed, indeed there are biases in the simulation programming that favor bacteria that have certain characteristics.

2 Legionellosis

2.1 Legionellosis disease

Clinical description Human legionellosis is a form of bacterial pneumonia of varying severity, sometimes fatal. Signs and symptoms includes high to moderate fiver, cough, muscle pain, headaches, shortness of breath. Sometimes digestive disorders sucha as nausea, vomiting and diarrhea, as well as neurological disorders occur.
The signs of poor prognosis identified concern:

- use of assisted ventilation,
- advaced age,
- kidney disease,
- cancer,
- immunosuppression,
- prolonged delay in administering medication.

The dignostic is confirmed radiologically in front of an acute pneumonia of bacterial origin. The duration of the incubation of legionellosis (and therefore the period of exposure) varies from 2 to 10 days[2].

Bacteria transmission Bacteria[3] are transmitted to humans by aerosolization and less often by aspiration (to the lung) of colonized water. For now, relation between infection and water ingestion (to digestive organ) is not demonstrated.

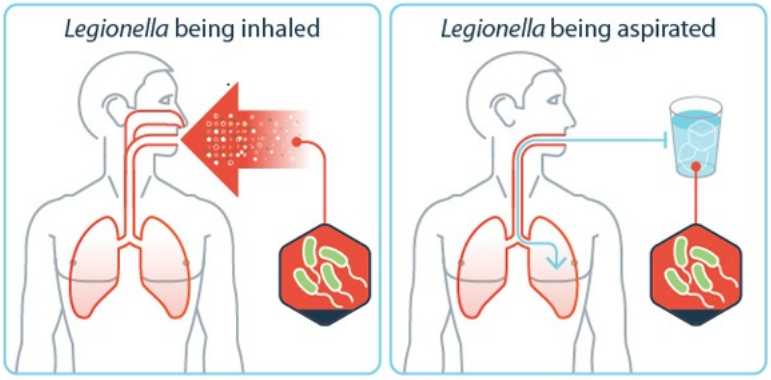


Figure 3: illustration of aspiration compared to inhalation
From Virginia departement of Health and Centers from Disease Control and Prevention

Pathophysiology The disease is caused by twenty of the 30 species of the identified group of bacteria (in 1991 [2]), now more than 60 spices have been identified**TO CITE**.

[2]During this time, the patient can transmit the disease whitout sign of any symptoms
[3]Bacteria is plurial of bacterium

Epidemiology Frequency of legionella pneumophila bacterium for community-acquired pneumonia is 0.5 to 10%[4].

2.2 Legionella pneumophila

The legionella pneumophila is the primary humanpathogenic bacterium ([it] represents 80% bacteria that cause legionellosis **CITE**) in this group and the causative agent of Legionnaires' disease [2] (other name of Legionellosis disease). This bacteira is thin, aerobic, pleomorphic, flagellated, non-spore forming and gram-negative bacterium of the genus Legionella.

Bacteria location The bacterium is found naturally in fresh water. It can also contaminate hot water tanks, cooling towers.

Detection The bacteria can be detected by immunofluorescence techiques. A fluorescent marker antibody come attach to the bacteria. This is a technique called indirect fluorescent antibody. Other tests like ELISA and microagglutination tests may be applied.
For clinical use, the appearance of simple diagnostic in urine tests has favored the search for specific antigens. It helped a lot in cluster discovery. Indeed, if there are much cases of legionellosis, there must be a source of bacteria somewhere near.

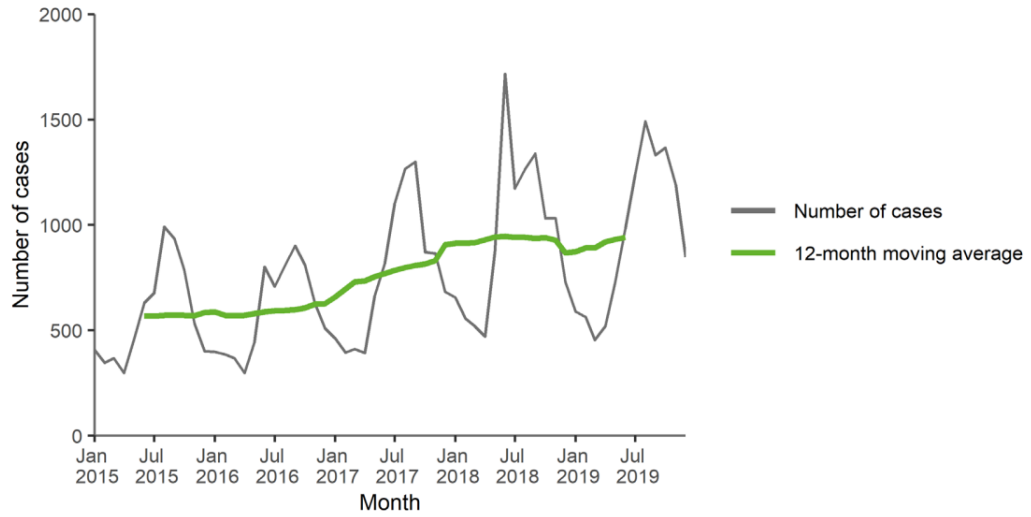
Biophysiology Legionella pneumophilia is a facultative intracellular parasite that can invade and replicate inside amoebae (a biological organism which has ability to alter its shape by extending and retracting pseudopods). Legionella pneumophilia bacteria uses these biological as reservoirs. They provide protection from stress from the environnement (e.g. chlorination of water, temperature).

Proliferation The bacteria has ability to proliferate on the walls of pipes (biofilms). L. pneumophilia can be aerolized throught showers, sprinklers and other fixtures which may leads to to infection (after prolonged exposure). When aerolized in mist aire, the bacteria can spread too.

Statistics This bacteria is the cause agent for most of the legionellosis disease. In the USA, there are approximately 3 infections with L. pneumophilia for 100 000 peoples each years. There are a peak in the summer. In endemic regions (regions where legionellosis disease is more present) about 4% to 5%. In France, in 2005, the compulsory declaration took into account 1527 cases of legionellosis representing 2 cases per 100,000 inhabitants[5]. On the next figure, you can see the distribution of legionnaires' disease in Europe.

Synthesis Legionella pneumophila is a bacterium that grows in water systems and is transmitted via aerosols. It is responsible for most bacterial pneumonia.

[4] it is a statistic that varies a lot depending on location and population criteria mainly
[5] Which is similar to USA statistics



Source: Country reports from Austria, Belgium, Bulgaria, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, the United Kingdom.

Figure 4: Distribution of Legionnaires' disease cases by month, EU/EEA, 2015–2019
Legionnaires' disease, Annual Epidemiological Report for 2019, European Center for Disease Prevention and Control

3 Simulating basics

3.1 Simulation framework

For now the simulation may be separated in 4 zones. The screen will be separated to display all 4 situations :

1. Control situation *(témoin in french)*,
2. Random characteristics situation,
3. Other random characteristics situation,
4. Another random characteristics situation.

Characteristics will be discussed in a specific section later

3.2 Simulation mechanics

Basics mechanics We don't simulate single bacteria (this is a "tactical" choice, if we use a micro-size = simulate bacteria one by one, we won't be able to properly stimulate macro-sized things i think) so we will have colony *$\cong$ item. The relation between them will be : for n size there will be 10^n bacteria (n the value of size).

Future mechanics goals Make the bacteria capacity randomized (after looking scientific article for accurate simulation) for "surviving" extreme situation (e.g. water at 90 degre celcius, frozen water)

Characteristics For now the characteristic is only by the size of item. For next step, we want to talk about the need for L. pneumophila in standing water to grow.

Next simulation objective The idea is to simulate different speeds of water flow. Indeed, if the biological organism is sufficiently adapted to develop in high-flow water, it may be necessary to modify the sanitary measures of channeling, conservation / treatment of water. This will be a first mechanic for simulating colony.

Future characteristics goals Other characteristics may be implemented, such as :

- Temperature (negative, low, ambient, high),
- Brightness/lighting or dark environment,
- Minimum colony size to allow for development.

The objective is to have mechanics relied to every of the previous characteristics so the bacteria can really "interact" with environment and the 4 (for now) different situation. The little problem for now is that the camera zoom reset after all refresh of the web page, and also the PC don't support more than 150 items size 1 or 2 moving and interacting : do each item may be a comlete colony and the size is relied (10^n bacteria for n size) to the number of bacteria ?

References

[1] S. Jarraud, M. Reyrolle, H. Meugnier, F. Forey, and J. Etienne. Légionellose. *la Presse Médicale Référence*, 2007.

[2] M Hong Nguyen, Janet E Stout, and Victor L Vu. Legionellosis. *Infectious disease clinics of North America*, 5(3):561–584, 1991.