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Bachelorthesis

Genome-scale metabolic modelling of *Acinetobacter baumannii* ATCC 17978

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1 Background and Motivation

Acinetobacter baumannii is a Gram-negative, non-motile opportunistic human pathogen with a short rod form (Fig. 1) [1]. It is one of the ESKAPE species (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter spp.*) [2] that causes severe infections with a high rate of morbidity and death due to its strong survival capacity and widespread habitats. The organism can also rapidly respond to changes in environment [3]. Therefore, it has an extraordinary capacity to develop resistance to multiple antimicrobial agents and antibiotics [4]. The use of antibiotics is often restricted to prevent the development of multidrug resistance in the organism that causes *A. baumannii* infections. This can also affect the development of other antimicrobials [5]. Coinfection with *A. baumannii* as a result of SARS-CoV-2 infections has been reported several times in the literature during the COVID-19 pandemic [6, 7, 8].

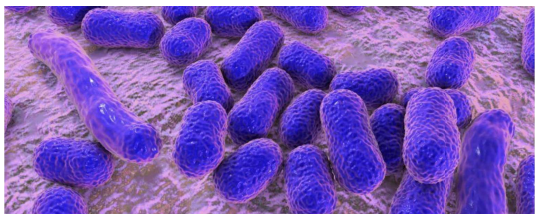

Figure 1 | 3D Figure of *Acinetobacter baumannii*. Image source: `https://www.hygiene-in-practice.de/pathogen/acinetobacter-baumannii/`

The strain ATCC 17978 is a clinical isolate from 1951, which was initially known as *Moraxella glucidolytica nonliquefaciens* [9]. Multiple pathogenicity islands, including as Type IV secretion systems, drug and heavy metal resistance proteins, and mobile elements, are found in its genome, which was sequenced in 2007 [10]. There are presently no models available for *A. baumannii* ATCC 17978 as of the beginning of this thesis. As a result, building a genome-scale metabolic model (GEM) of *A. baumannii* ATCC 17978 is of great interest and importance for future research. The new model should assist the researcher to comprehend better *Acinetobacter baumannii*.

2 Aim and Approach

During the group project in the lecture "System Biology I," an initial draft of *Acinetobacter baumannii* was developed. However, the model had several inconsistencies with experimental data; for example, when the uptake of oxygen was limited, the model of an aerobic bacterium showed a reduced growth rate rather than no growth.

Following the protocol for developing a high-quality genome-scale metabolic reconstruction [11], the model will be progressively refined. The goal is to develop a high-quality genome-scale model of *A. baumannii* ATCC 17978 and compare it to the models of other strains (e.g., *A. baumannii* ATCC 19606 or AYE). Meanwhile, the usage of different methods during the simulation of the model will also be compared, such as the comparison between two generally used approaches in predicting the growth rate and determining the set of essential genes, Flux Balance Analysis (FBA)[12] and minimization of metabolic adjustment (MOMA)[13].

3 Requirements

(1) Fundamental understanding of biochemistry, (2) interest in systems biology, particularly in constraint-based modeling, (3) basic knowledge of Python programming, (4) capability of using COBRApy [14] and Biology Markup Language (SBML) [15], and (5) interest in learning the usage of other tools during the model reconstruction (e.g., CarveMe [16], MEMOTE [17]).

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