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Masterthesis

Reconstruction of a metabolic model of *Proteus vulgaris*

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1 Background and Motivation

Proteus vulgaris is a Gram-negative, rod-shaped, facultatively anaerobic genus of bacteria. Its motility is enabled by peritrichous flagella [1]. Hauser first described it in 1885, who observed an intensive swarming growth of the bacillus in culture medium and liquefaction of gelatin. Later, in 1978, the bio-group 1 of *P. vulgaris* was defined by Brenner et al.

P. vulgaris is mainly found in the human gut [4] but can also be found in various environments, including the nasal cavities [5]. *P. vulgaris* is often described as opportunistic, leading to various infections, including urinary tract, respiratory tract, wound, and skin infections [6]. The virulence factors of *P. vulgaris* lead to host cell invasion and cytotoxicity. Additionally, these factors can also induce urease enzymes, which lead to bladder and kidney stones [7]. In a study from 2013, Bahashwan and El Shafey found that *P. vulgaris* accounts for 3 % of the annual infection cases while having resistance to multiple antibiotics [8, 4]. Besides resistances to specific clinical antibiotics, *P. vulgaris* is, according to Wang et al., the first naturally occurring Gram-negative bacterium with the *cfr* gene [9]. This gene results in bacterial resistance to 8 classes of antibiotics.

Figure 1 | After 24 hours, this inoculated MacConkey agar culture plate cultivated colonial growth of Gram-negative, rod-shaped, and facultatively anaerobic *Proteus vulgaris* bacteria. Picture source: `https://de.wikipedia.org/wiki/Datei:Proteus_McConkey.jpg`

As of the start of the thesis, there are currently no models available for *P. vulgaris*. A computer model to simulate the growth might allow for new insights as to what leads to the swarming growth and possible future medications besides antibiotics.

2 Aim and Approach

This thesis focuses on the molecular mechanisms of *P. vulgaris* growth. The aim is to create a high-quality systems biology model of *P. vulgaris*, which grows in the simulated media of the gut, nasal cavities, and skin. Since there are no available models at the start of the thesis, the steps will follow the standard operating procedure of the Computational Systems Biology (CSB) research group and commonly accepted guidelines [10]. These steps will include: (a) analyzing the created model, (b) conducting literature research to identify the bacterium's growth conditions, (c) identifying potential gaps in the metabolic network, (d) defining test cases to check the correctness of the model, (e) running simulations, and (f) aligning the model with available data from experimental investigations.

3 Requirements

(a) Understanding of biochemistry and molecular mechanisms, (b) interest in systems biology, basic knowledge of Python programming, (c) attentivity for details, and (d) interest in learning Biology Markup Language [11], MIRIAM annotations [12], and the Systems Biology Ontology [13].

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