

Bachelor Thesis

Analyzing the metabolic phenotypes of *S. capitis* using constraint-based modeling

Anna Lefarova

January 30, 2023

Mentor: M. Sc. Nantia Leonidou

Supervisor: Jun.-Prof. Dr. Andreas Dräger

1 Background and Motivation

Staphylococcus capitis (see Figure 1) belongs to the family of coagulase-negative staphylococci (CoNS). *S. capitis* was primarily studied as an opportunistic pathogen of the human skin [2]. Generally, Staphylococci represent the omnipresent microbiota of human skin and mucous membranes and can cause various hospital-acquired infections. A study from 2016 shows that *S. capitis* was present in over 75 % of patients on admission by investigating the composition of the nasal staphylococcal microbiome [3]. Moreover, it has subsequently been found in neonatal intensive care units (NICUs) in 17 countries and identified as a cause of Late-Onset Sepsis (LOS) in neonates [4].

Bacterial persistence in hospitals can be explained by the ability of *S. capitis* to adhere to environmental surfaces by producing biofilm that confers protection against environmental stresses [5]. Recently the bacterial physiology and resistance behavior of *S. capitis* under spaceflight-specific conditions was studied. To verify if spaceflight induced physiological changes, three spaceflight-relevant isolates were compared with the type strain DSM 20326 [6].

At the moment, two models (strains QN1 and CR0101) for *S. capitis* created in an automated way are available in the Virtual Metabolic Human (VMH) database [7]. Creating a manually curated genome-scale metabolic model (GEM) should contribute to a deeper understanding of the metabolic network of *S. capitis* and is of great interest to future research.

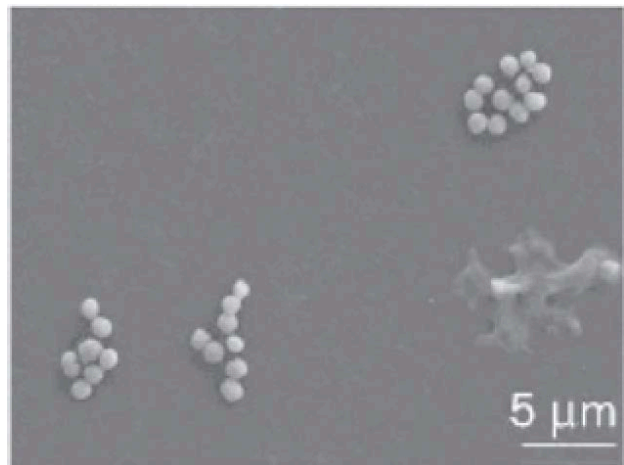


Figure 1 | Scanning electron microscopy of the clinical isolate of *Staphylococcus capitis* grown in glucose-enriched trypticase soy broth (TSBg) [1].

2 Aim and Approach

The strain that this thesis will focus on is the H17 which was isolated from a forehead skin swab at the Institute for Aerospace medicine at the German Aerospace Center (DLR, Cologne, Germany)¹.

The aim is to create a high-quality systems biology model of *S. capitis* and compare it to the existing autonomously created reconstructions. The draft reconstruction model will be created with CarveMe [8] and manually curated using experimental phenotypic data obtained from DLR. For the gap-filling, different tools will be compared, such as COBRApy and NICEgame [9]. Each step will be validated with the quality control Python software named MEMOTE [10] to ensure the quality of the model.

Future work comprehends an extension of the model to include biofilm production by *S. capitis* and builds further strain-specific models for the rest of the strains.

3 Requirements

Motivation and interest to learn more about systems biology and constrained-based modeling in particular. Fundamental understanding of biochemistry and ability to interpret experimental data. Basic knowledge of Python programming and ability to use and combine results from different bioinformatics tools and packages.

References

- [1] Valerie S. Greco-Stewart et al. “Biofilm formation by *Staphylococcus capitis* strains isolated from contaminated platelet concentrates.” In: *Journal of medical microbiology* 62.7 (2013), pp. 1051–1059. DOI: 10.1099/jmm.0.050500-0.
- [2] Wesley E. Kloos and Karl H. Schleifer. “Isolation and characterization of staphylococci from human skin II. descriptions of four new species: *Staphylococcus warneri*, *Staphylococcus capitis*, *Staphylococcus hominis*, and *Staphylococcus simulans*1.” In: *International Journal of Systematic and Evolutionary Microbiology* 25.1 (1975), pp. 62–79. DOI: 10.1099/00207713-25-1-62.
- [3] Claire L. McMurray, Katherine J. Hardy, Szymon T Calus, Nicholas J. Loman, and Peter M. Hawkey. “*Staphylococcal* species heterogeneity in the nasal microbiome following antibiotic prophylaxis revealed by tuf gene deep sequencing.” In: *Microbiome* 4.1 (2016), pp. 1–8. DOI: 10.1186/s40168-016-0210-1.
- [4] Heather M. Felgate et al. “Characterisation of neonatal *Staphylococcus capitis* NRCS-A isolates compared with non NRCS-A *Staphylococcus capitis* from neonates and adults.” In: *bioRxiv* (2022). DOI: 10.1101/2022.12.02.518718.
- [5] Marie Chavignon et al. “Environmental Persistence of *Staphylococcus capitis* NRCS-A in Neonatal Intensive Care Units: Role of Biofilm Formation, Desiccation, and Disinfectant Tolerance.” In: *Microbiology Spectrum* 10.6 (2022), e04215–22. DOI: 10.1128/spectrum.04215-22.
- [6] Katharina Siems et al. “Phenotypic and genomic assessment of the potential threat of human spaceflight-relevant *Staphylococcus capitis* isolates under stress conditions.” In: *Frontiers in Microbiology* 13 (2022), p. 1007143. DOI: 10.3389/fmicb.2022.1007143.
- [7] Alberto Noronha et al. “The Virtual Metabolic Human database: integrating human and gut microbiome metabolism with nutrition and disease.” In: *Nucleic acids research* 47.D1 (2019), pp. D614–D624. DOI: 10.1093/nar/gky992.
- [8] Daniel Machado, Sergej Andrejev, Melanie Tramontano, and Kiran Raosaheb Patil. “Fast automated reconstruction of genome-scale metabolic models for microbial species and communities.” In: *Nucleic acids research* 46.15 (2018), pp. 7542–7553. DOI: 10.1093/nar/gky537.
- [9] Evangelia Vayena et al. “NICEgame: A workflow for annotating the knowledge gaps in metabolic reconstructions, using known and hypothetical reactions.” In: *bioRxiv* (2022). DOI: 10.1101/2022.02.10.479881.
- [10] Christian Lieven et al. “MEMOTE for standardized genome-scale metabolic model testing.” In: *Nature Biotechnology* (3 Mar. 2020). ISSN: 1546-1696. DOI: 10.1038/s41587-020-0446-y.

¹The DLR Institute of Aerospace Medicine – <https://www.dlr.de/me/en/>