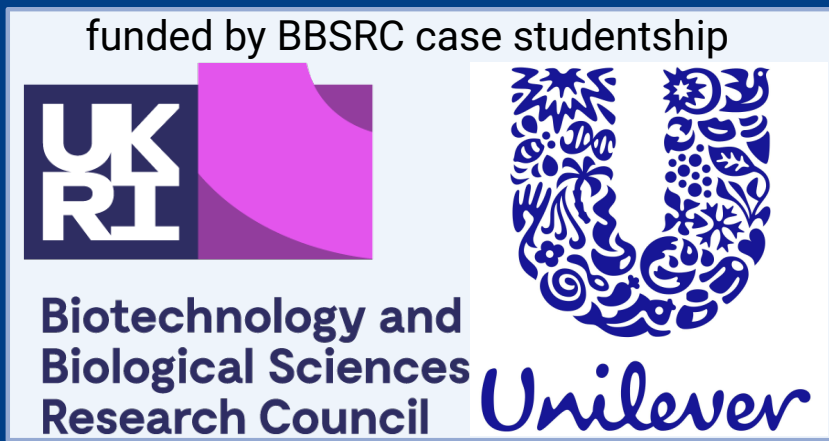


Reconstructing metabolic models of oral bacteria to investigate acidification and caries progression

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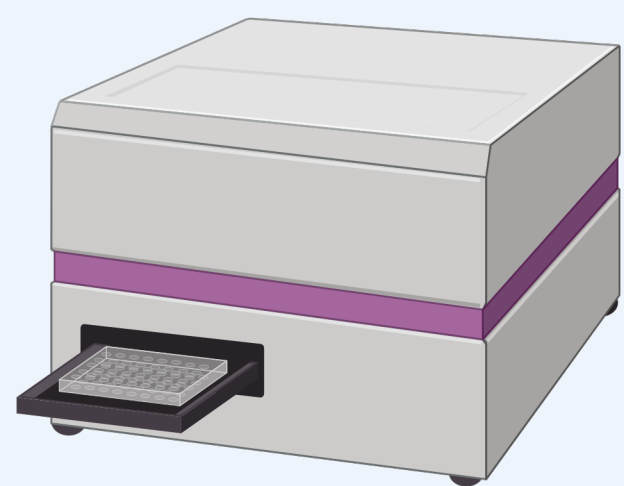
VISION

The aim of my research is to develop a community metabolic model of the five oral bacterial species to understand the impact of pH on the kinetics and interaction of the oral bacterial community, validated using experimental data.

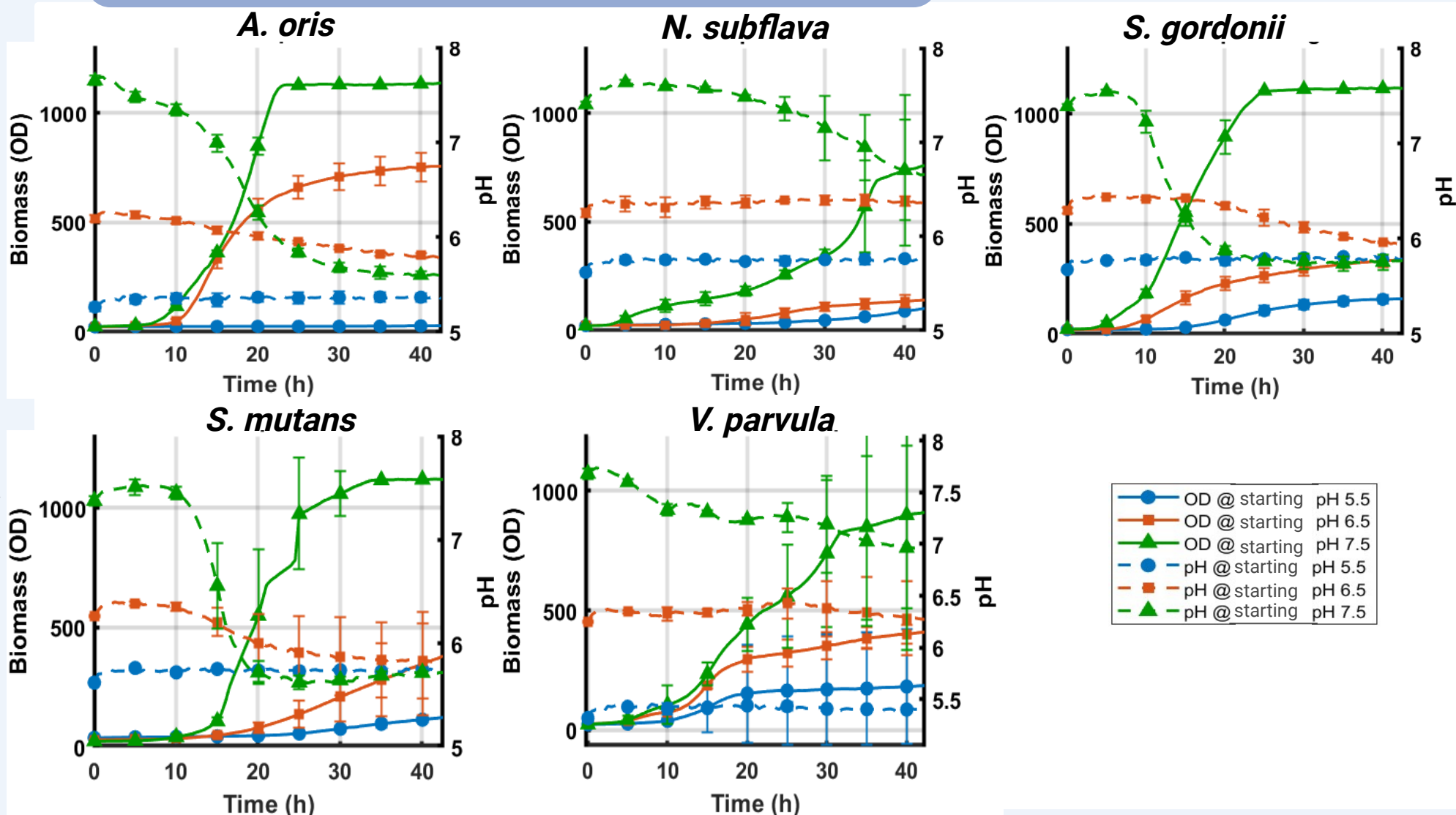
BACKGROUND

- The oral cavity is composed of a complex community of microorganisms interacting both physically and chemically. The metabolic activity of acid-producing bacteria lowers the local pH within the dental biofilm and contributes to caries.
- To better understand metabolic interactions leading to acid production, four early colonizers of dental plaque - *Streptococcus gordonii*, *Actinomyces oris*, *Neisseria subflava*, and *Veillonella parvula* along with the caries-associated species *Streptococcus mutans* have been characterized experimentally for growth together in a chemically defined Amended Fortified M1 Medium with Citrate (AFMC) medium [1,2].
- Genome scale metabolic models (GEMs) were developed for each species to characterise the metabolic pathways for production of Volatile fatty acids (VFAs) and consequent pH changes.

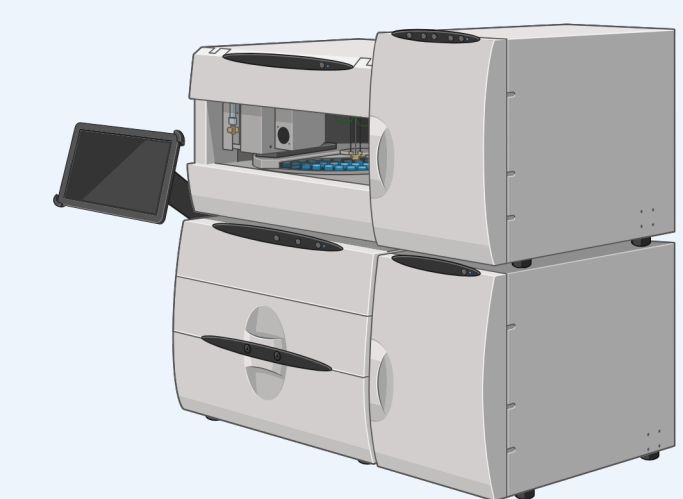
Wet - Lab



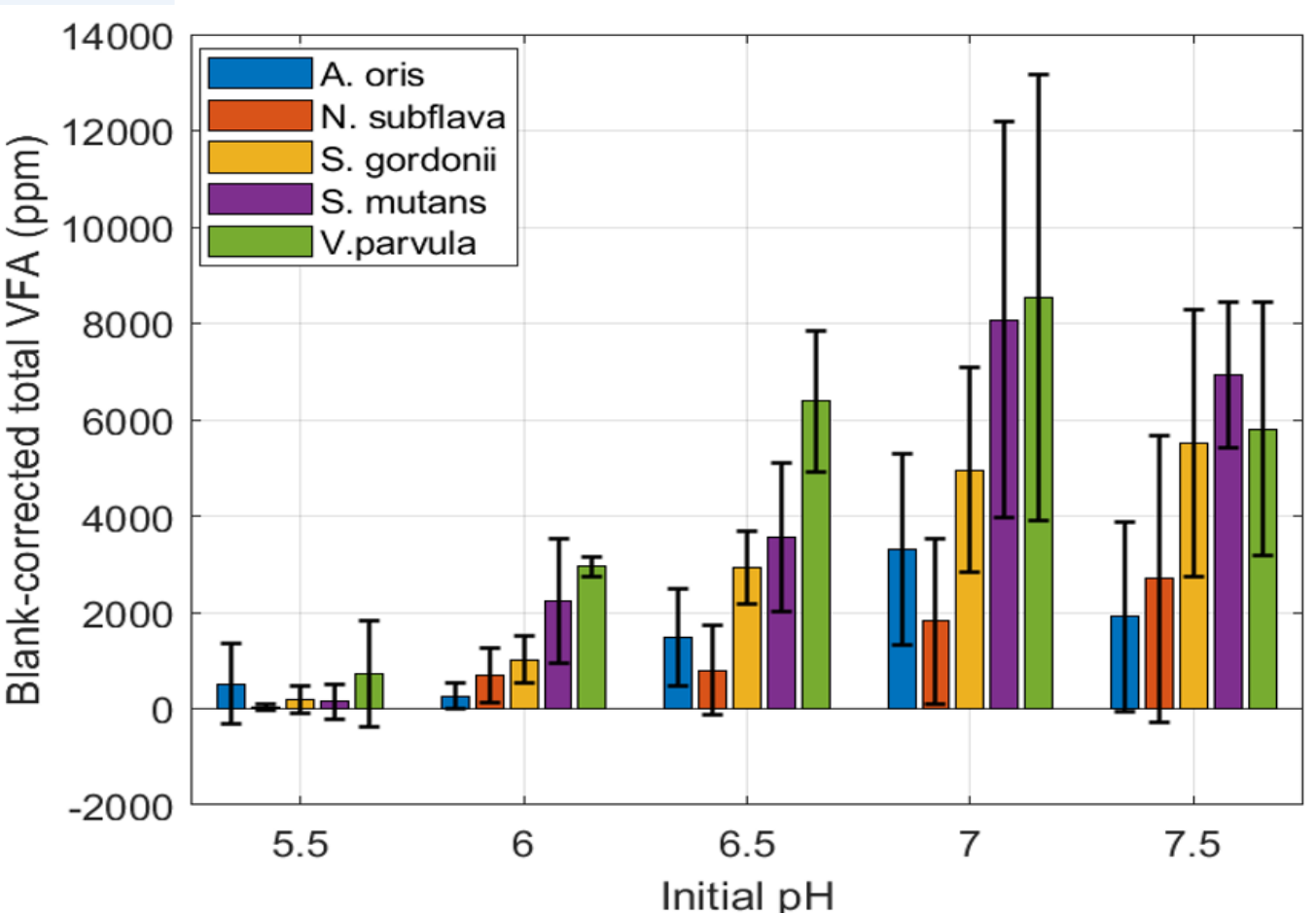
Growth at different pH was measured using a Biolector plate reader with continuous pH measurement.



All the bacteria grew at pH 7.5 and 6.5 in AFMC media and had the slowest growth at pH 5.5. The pH dropped below 6 from the growth of *S. mutans*, *S. gordonii* and *A. oris*



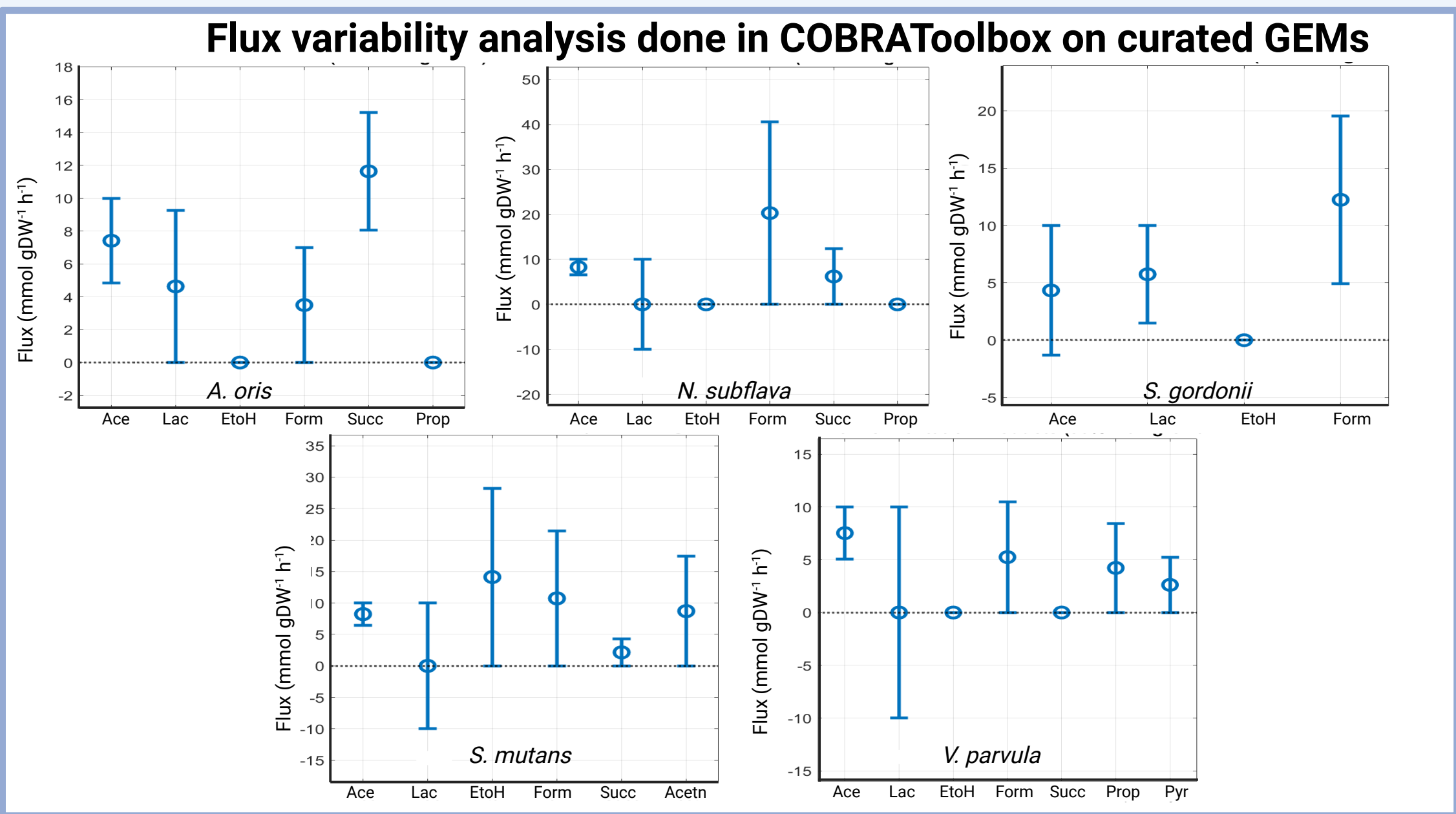
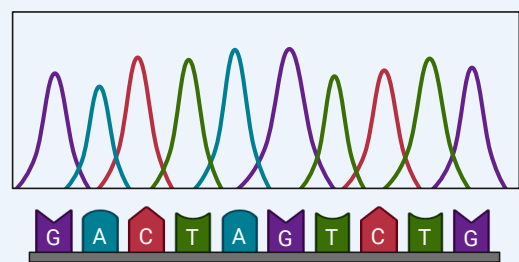
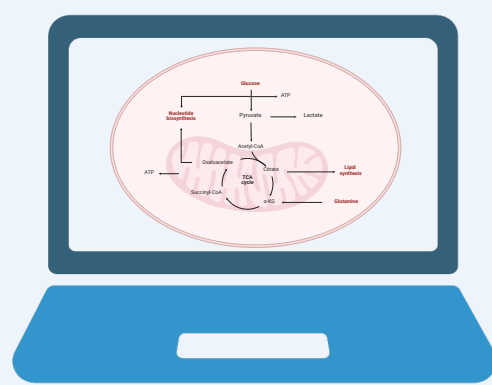
Quantification of VFAs- acetate, formate and propionate by ion chromatography following growth at different pH.



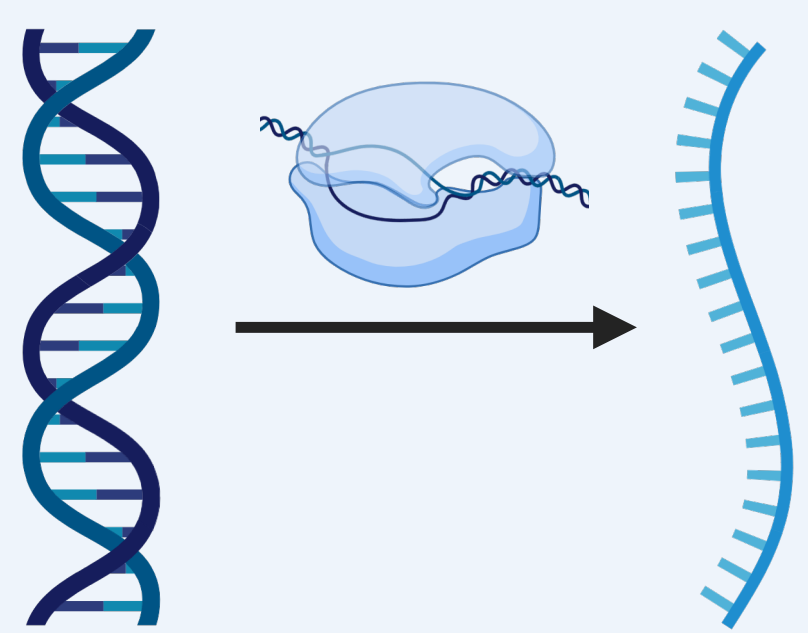
The maximum VFAs were produced near neutral pH for all species.

In - Silico

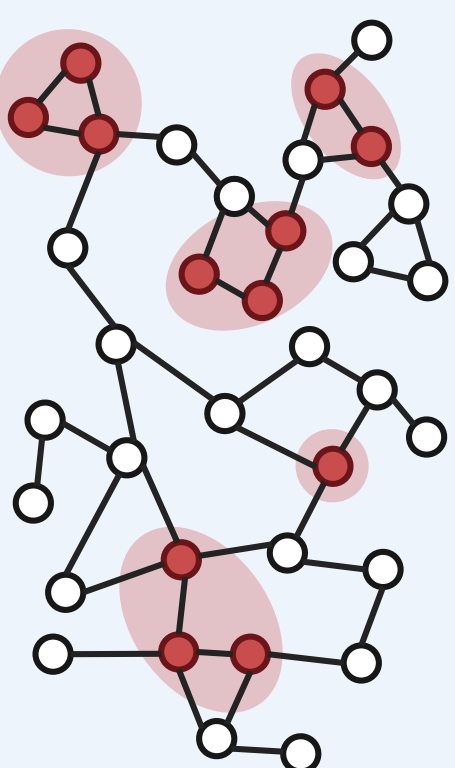
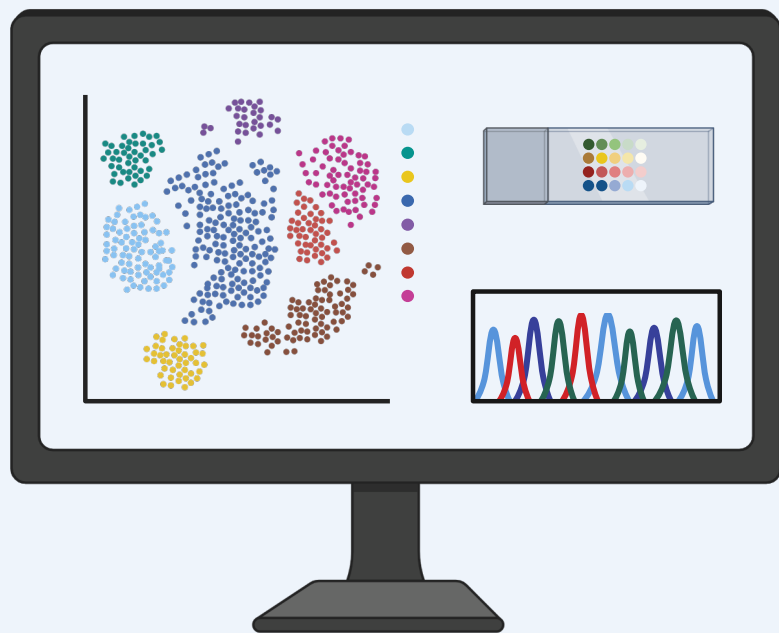
The genomes of the strains were sequenced, annotated and the GEMs were drafted and gap-filled with AFMC media using RAST and ModelSEED2 pipelines. The model was then curated using DEMETER for flux balance analysis in the COBRA Toolbox[3,4].



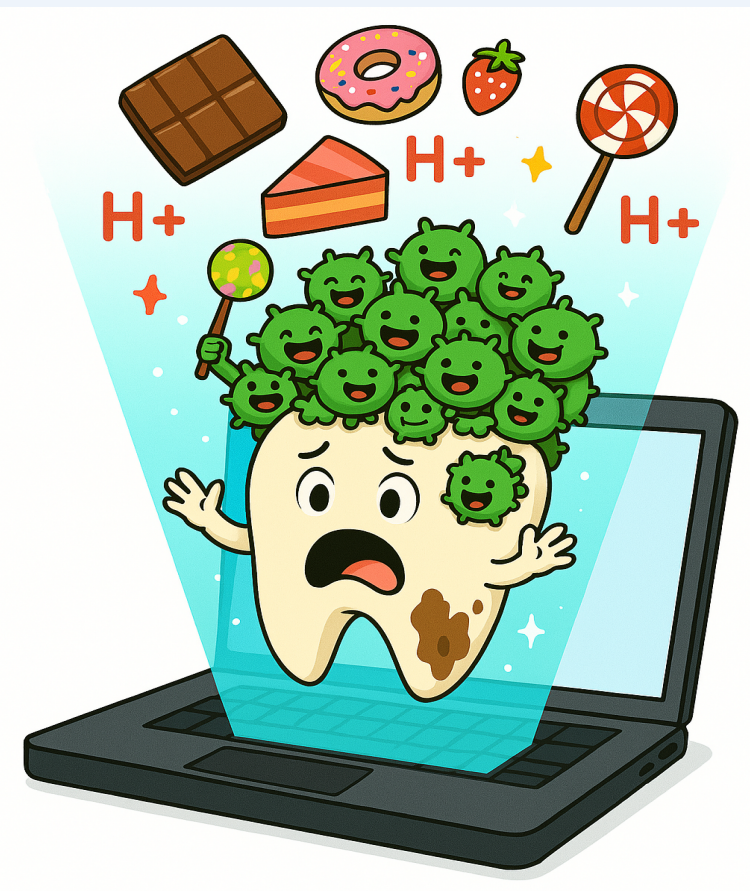
- The metabolites detected experimentally were matching the positive fluxes predicted by flux variability analysis, validating the acid production pathways of the GEMs.
- The acid metabolism and secretion profiles are species specific and in agreement with the literature, e.g. *V. parvula* is predicted to be able to metabolise lactate and produce acetate and propionate, as also confirmed experimentally in the AFMC medium [6]



The individual models will be further constrained with transcriptomic data for fermentation pathways



The individual GEMs can be combined to build community metabolic models. Wet-lab measurements of VFA production, fermentation kinetics, and transcriptomic profiles will be incorporated into the modelling framework to characterise the effect of pH on community metabolism.



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1. Sangha, J.S., et al., Effects of glucose and lactate on *Streptococcus mutans* abundance in a novel multispecies oral biofilm model. *Microbiol Spectr*, 2024, 12(4). 2. Sangha JS et al., Advancing dental biofilm models: the integral role of pH in predicting *S. mutans* colonization; 2025. mSphere 10:e00743-24. 3. Arkin, A.P., et al., KBase: The United States Department of Energy Systems Biology Knowledgebase. *Nat Biotechnol*, 2018, 36(7): p. 566-569. 4. Hyduke, D., et al., Creation and analysis of biochemical constraint-based models using the COBRA Toolbox v.3.0. *Protocol Ex change*, 2011. 5. Heinken, A., Refinement of genome-scale reconstructions through the DEMETER pipeline. 2021. 6. Ng SKC, Hamilton IR. Lactate Metabolism by *Veillonella parvula*. *J Bacteriol*; 1971.