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

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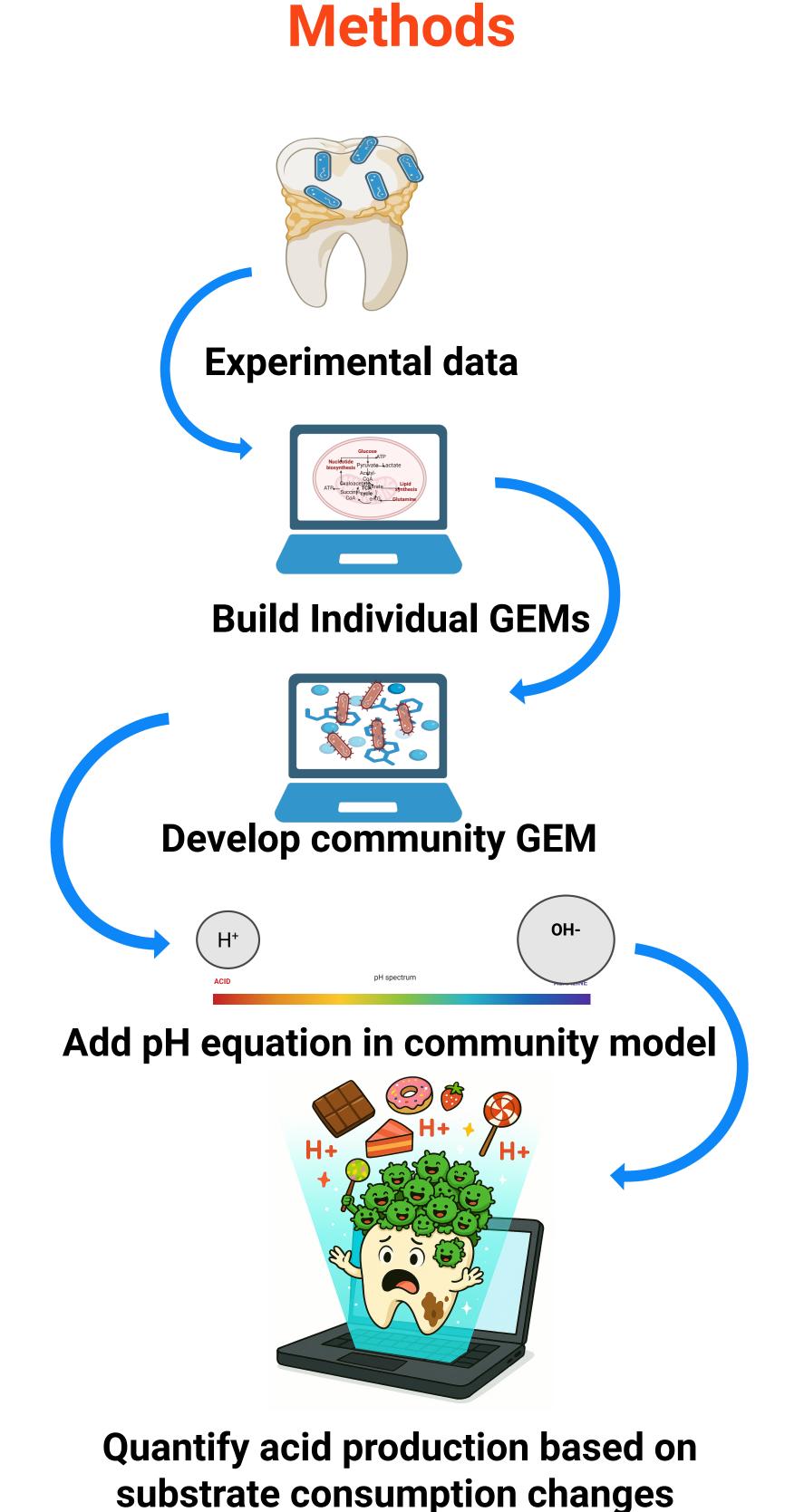
Background

The oral cavity is composed of a complex community of microorganisms interacting both physically and chemically. The metabolic activity of acid-producing bacteria such as *Streptococcus mutans* lowers the local pH within the dental biofilm and contributes to caries. To better understand these metabolic interactions, genome-scale metabolic models (GEMs) have been developed of four early colonizers of dental plaque – *Streptococcus gordonii*, *Actinomyces oris*, *Neisseria subflava*, and *Veillonella parvula* – along with the caries-associated species *Streptococcus mutans*, in a chemically defined, Amended Fortified M1 Medium with Citrate (AFMC) (Sangha et al., 2024).

Vision

TThe aim of my research is to develop a community metabolic model for the five oral bacterial species to understand the impact of abiotic factors like pH on the kinetics and interaction of oral bacterial species.

Methods

Experimental data

Build Individual GEMs

Develop community GEM

Add pH equation in community model

Quantify acid production based on substrate consumption changes due to community interactions

Results

Wet lab

1. All the bacteria were able to grow at pH 7.5 and 6.5 in AFMC media and had the slowest growth at pH 5.5 due to an acidic environment. The pH dropped below 6 from the growth of *S. mutans*, *S. gordonii* and *A. oris* (Fig. 1).

2. Most strains produced acetate and formate as the fermentation product. *V. parvula* also produced propionate (Fig. 2).

Fig. 1 Growth curves of bacterial strains and resulting change in pH over time under different starting pH conditions.
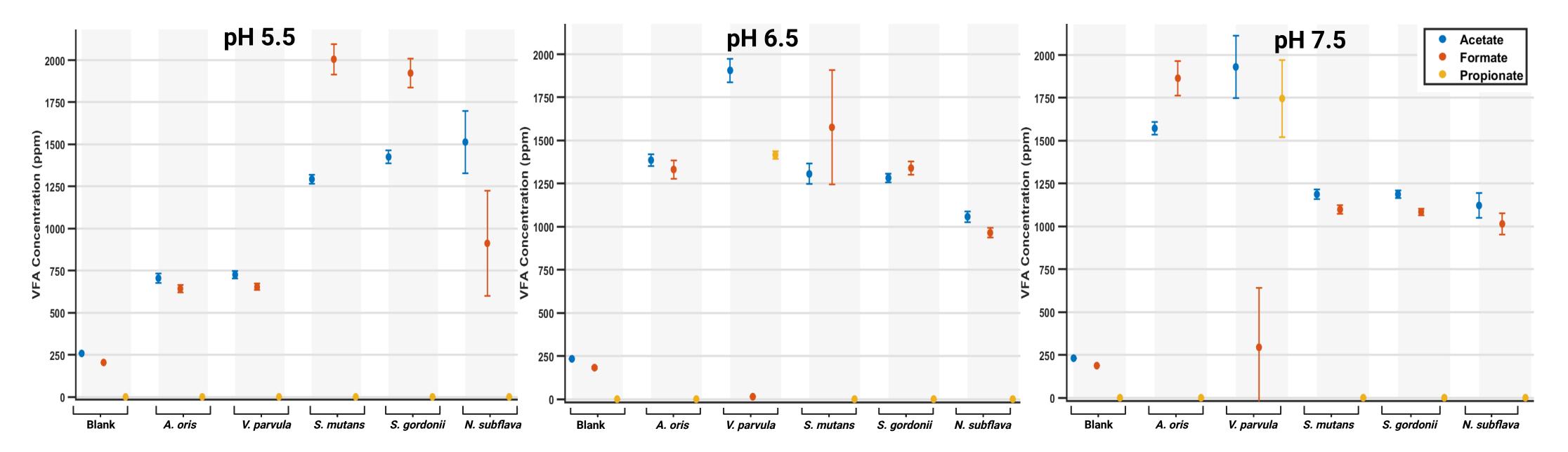

Fig. 2 Quantification of volatile fatty acids (VFA) acetate, formate and propionate by ion chromatography following growth at different pH values.

In silico

1. 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 media was supplemented with ions to enable biomass production within the KBase framework (Arkin et al., 2018).
2. Manual curation was done to restore heme biosynthesis, enabling biomass growth in the COBRA toolbox (Hyduke et al., 2011).
3. The models were gap-filled using Demeter pipeline with strain specific experimental data to restore blocked pathways and ATP production Fig. 3 and 4 (Heinken et al., 2021).
4. This also balanced the charge and mass of the models by up to 97% (Fig. 4).
5. The models will be further combined to develop a community model.

Draft models developed using ModelSeed2

Manual curation for positive Biomass

Experimental data collection

Gap-filled using Demeter
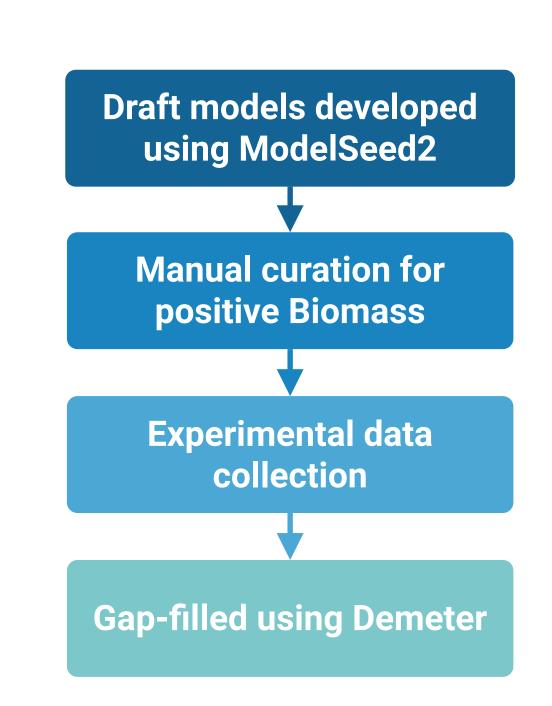
Fig. 3 Flow diagram of how the draft models were refined.

Fig. 4 Biomass and ATP production of the GEMs after gap-filling. Both were improved and the mass and charge of the models were balanced

References

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2. Arkin, A.P., et al., KBase: The United States Department of Energy Systems Biology Knowledgebase. *Nat Biotechnol*, 2018. 36(7): p. 566-569.
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