

# *i*PACH22FFG

A Genome-Scale Model For *Cutibacterium acnes* Within The Human Nose

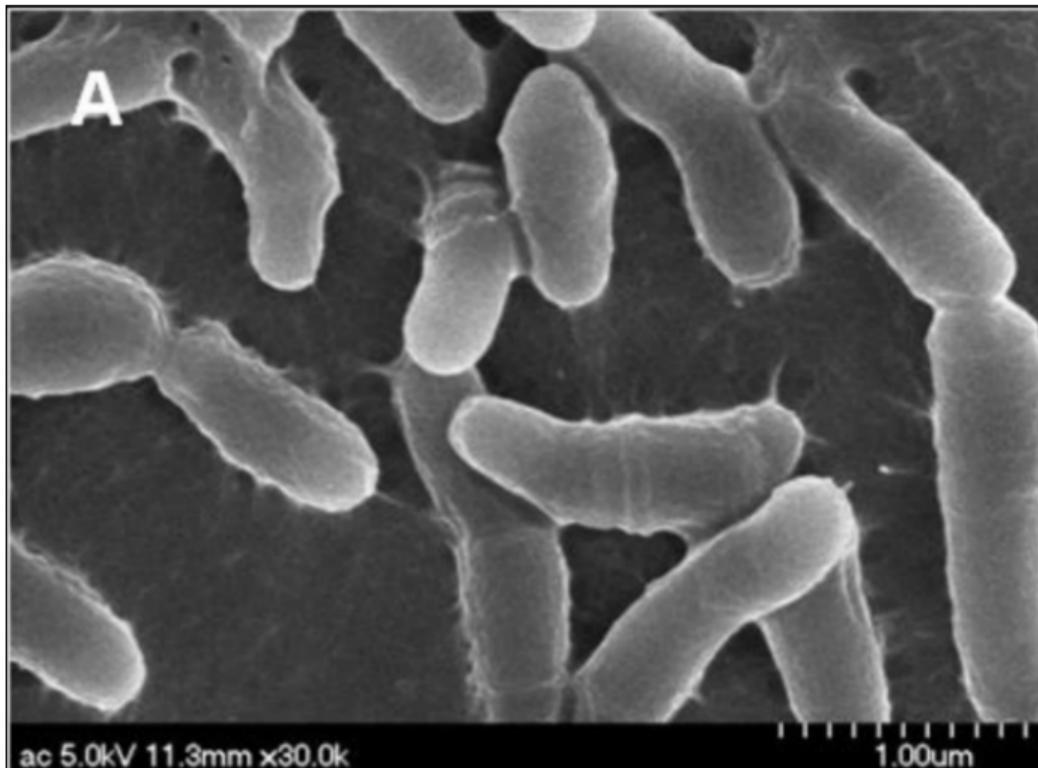
Simon Frank    Tobias Fehrenbach

Systems Biology I Project, 03.02.2022

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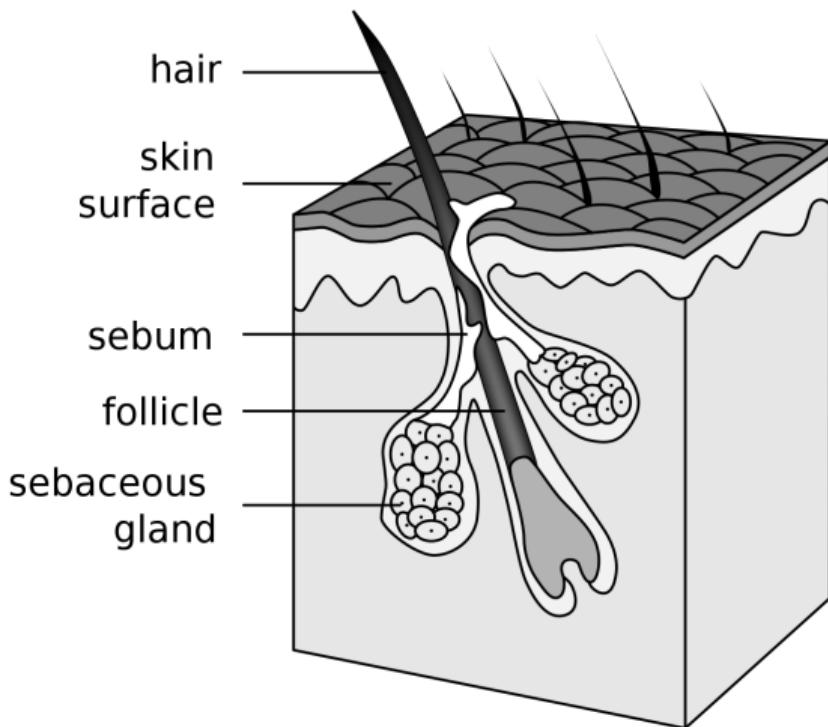
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# Cutibacterium acnes



- formerly *Propionibacterium*
- non-sporulating, gram-positive, slow-growing facultatively anaerobic
- commensal skin bacteria

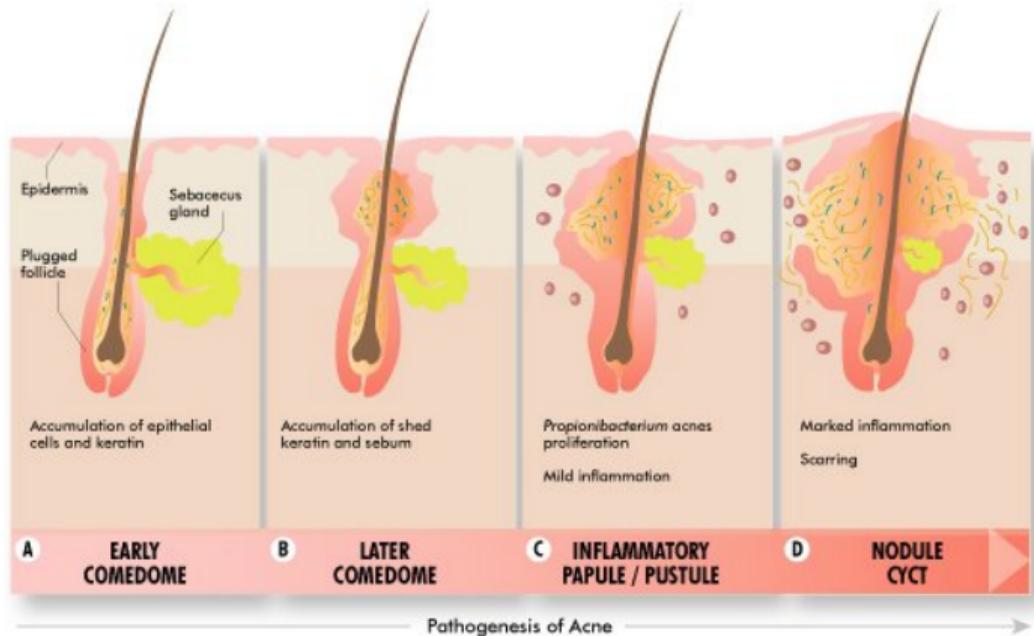
## C. acnes - Appearance



Sebaceous gland - Wikipedia [2021]

- Most common appearance: human skin, despite other: oral cavity, gastrointestinal & genitourinary tract
- part of the commensal microbiome (<2% of all bacteria)
- only bacteria to colonize sebaceous follicles, due to ability to hydrolyze triglycerides → lowering sebum pH, inhibiting pathogenic bacteria

# C. acnes - Infections - Acne vulgaris, name giving disease

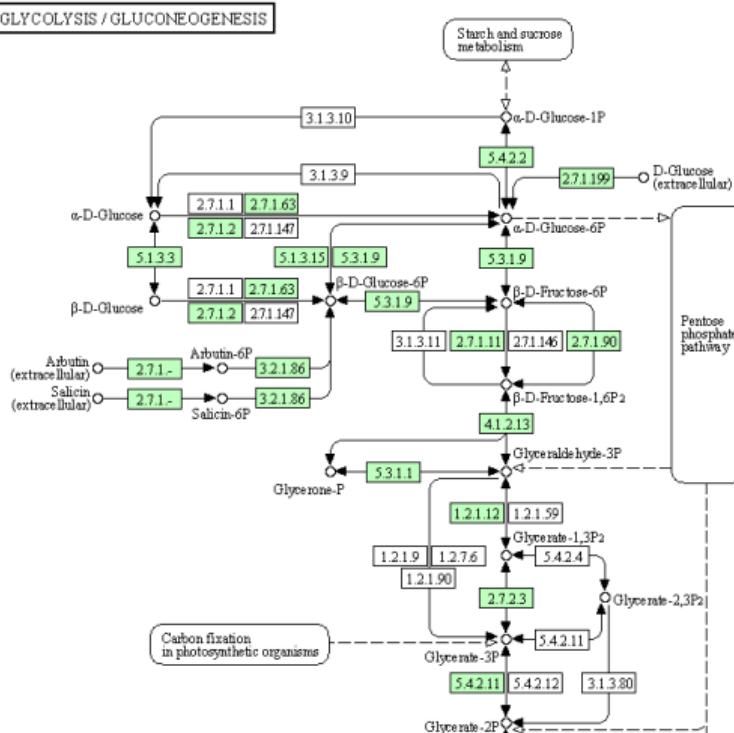


Elan Medical Skin Clinic LTD [2022]

pcds.org.uk [2022]

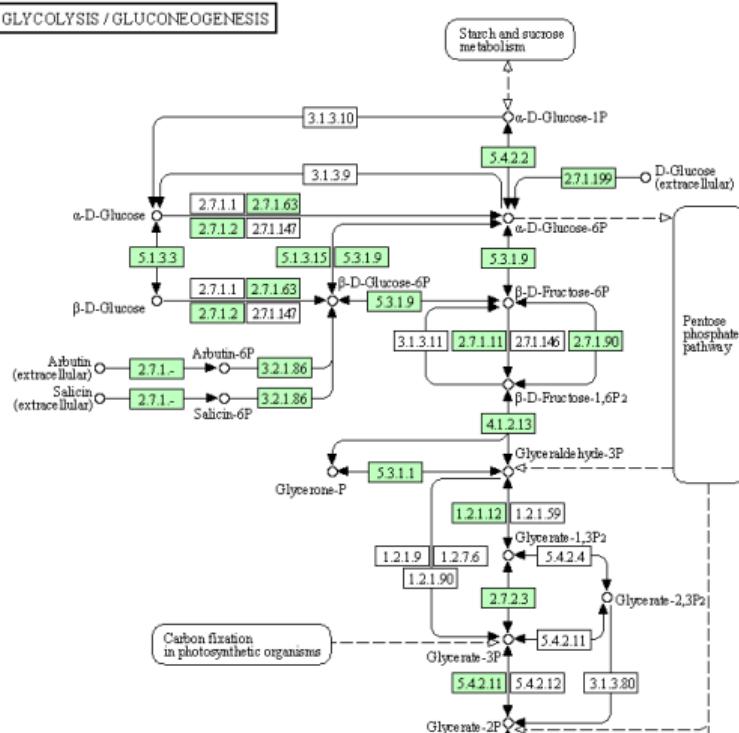


## C. acnes - Infections



- causes multiple other diseases upon entry to the body (endocarditis, septic arthritis, sarcoidosis)
- causal agent of 51% of post-surgical shoulder infections
- increased importance in healthcare-associated infections (HAIs) due to acquisition of antibiotic resistances

# GEMs and HALs

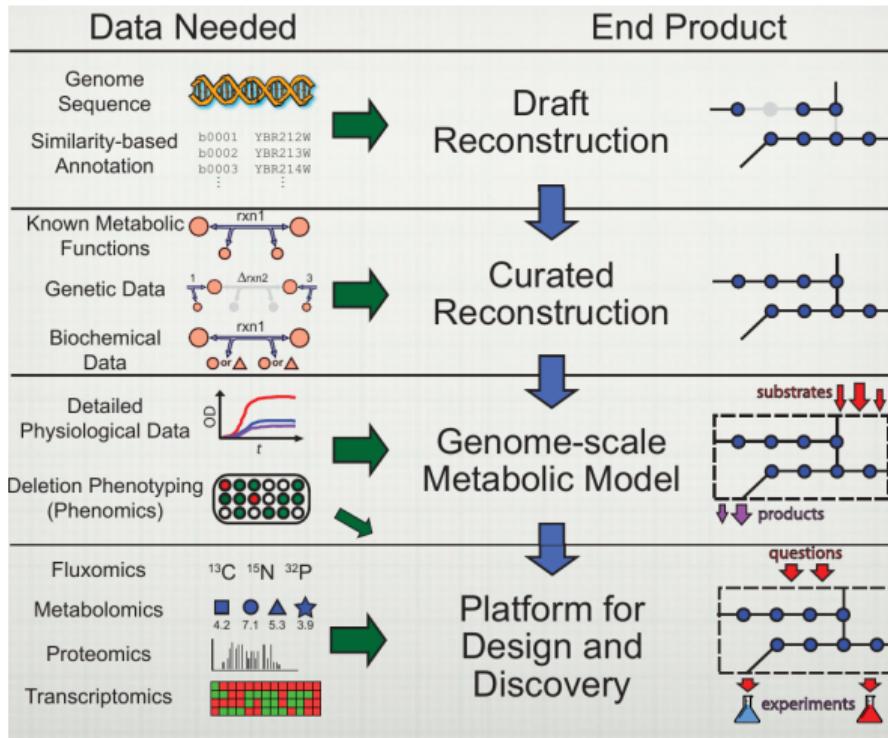


- HAI associated pathogen research often difficult and expensive
- Genome-associated models are a modern way to research microbes *in silico*
- e.g. to simulate effectiveness of new antibiotics, microbiome interactions within the human nose, virulence

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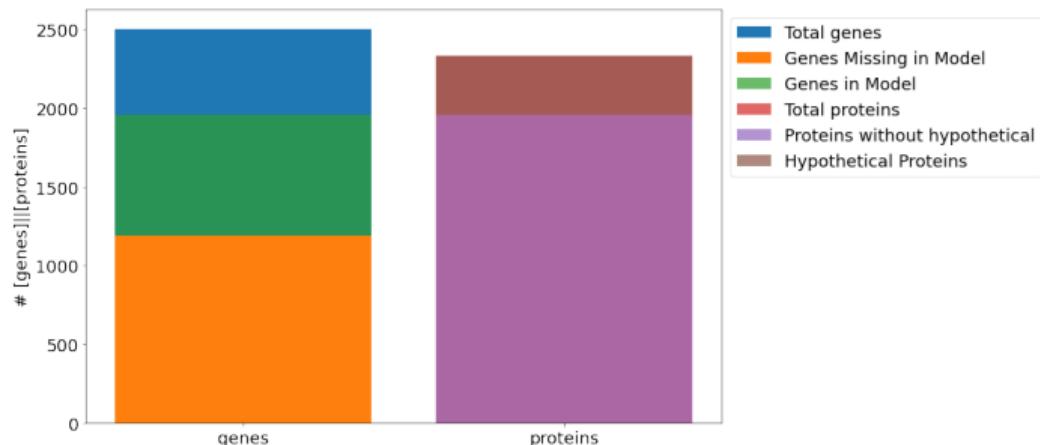
# GEM - Bottom-up reconstruction



Dräger [2021]

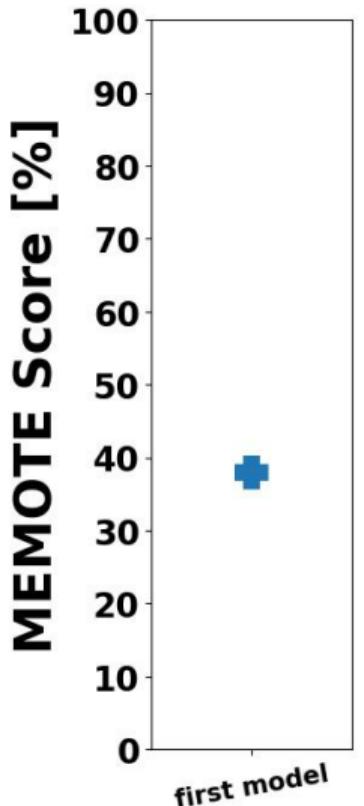
# Draft Reconstruction with CarveMe

Comparing genes and proteins in the model vs stated by the NCBI



- carved from protein FastA provided by the NCBI, strain: HL096PA1
- First model contained: 1759 reactions, 1230 metabolites and 769 (36 essential) genes
- maximal growth rate:  $35.40 \frac{mmol}{gDW \cdot h}$

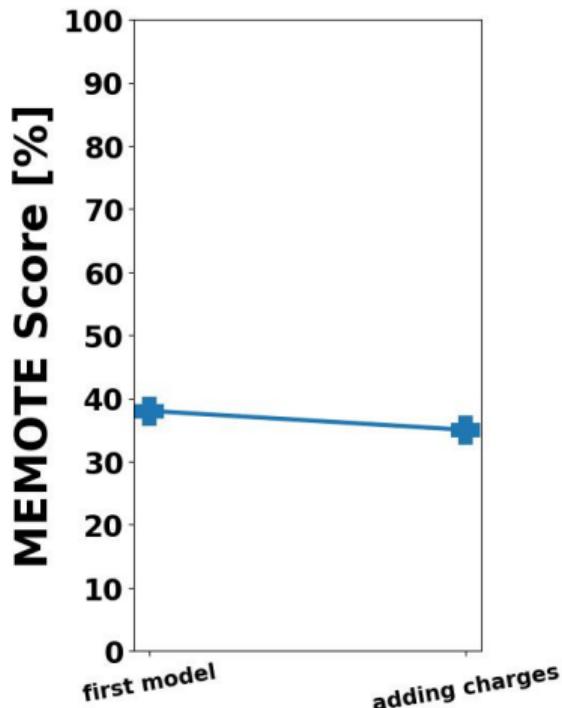
# First evaluation with MEMOTE



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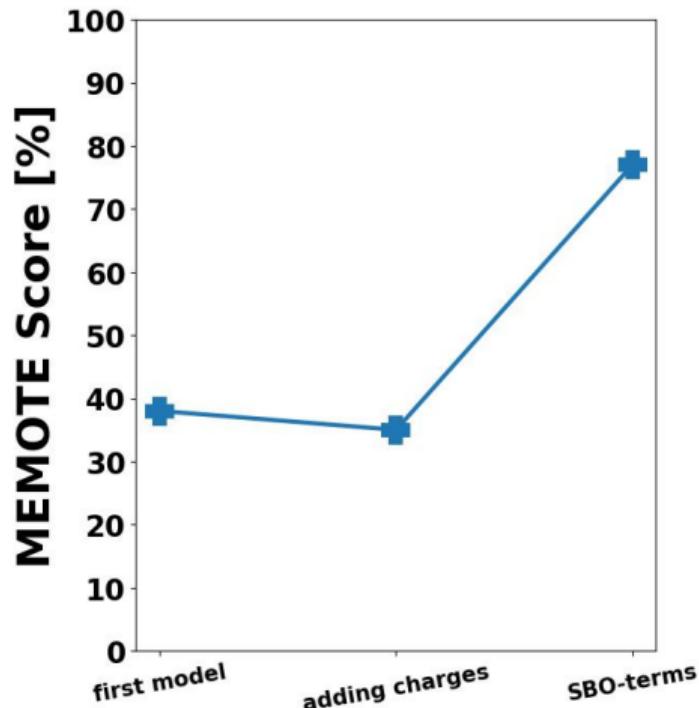
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# Adding charges



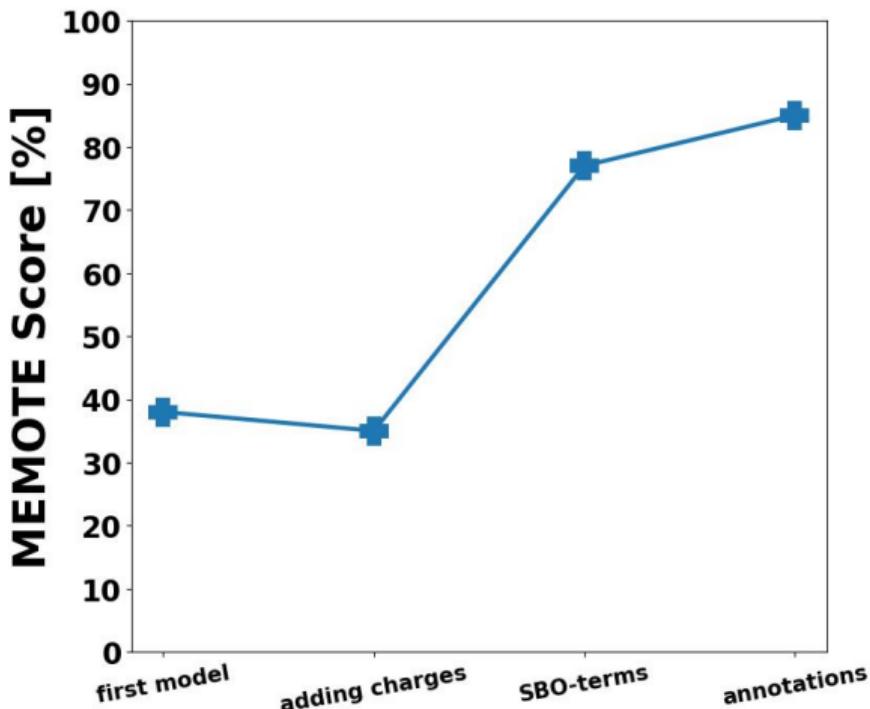
- lowered the MEMOTE score because of imbalances

# Adding SBO-Terms



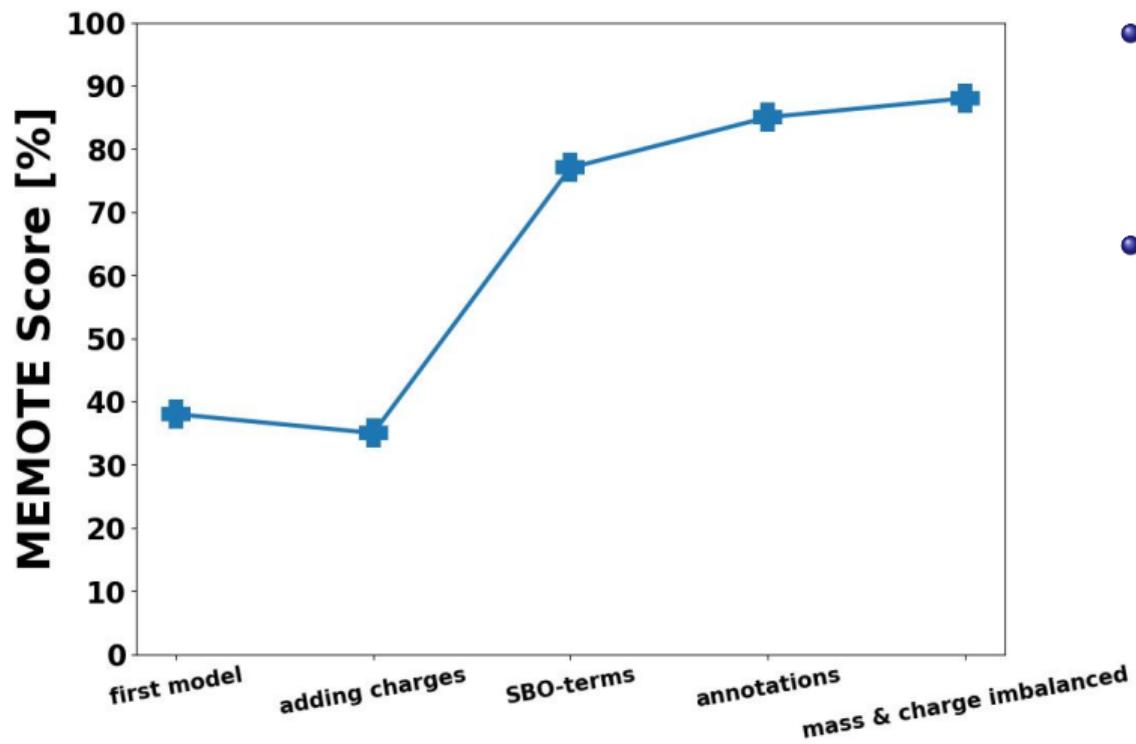
- Huge increase ( $\sim 37\%$ )
- Indicates importance of SBO terms

# Adding other annotations



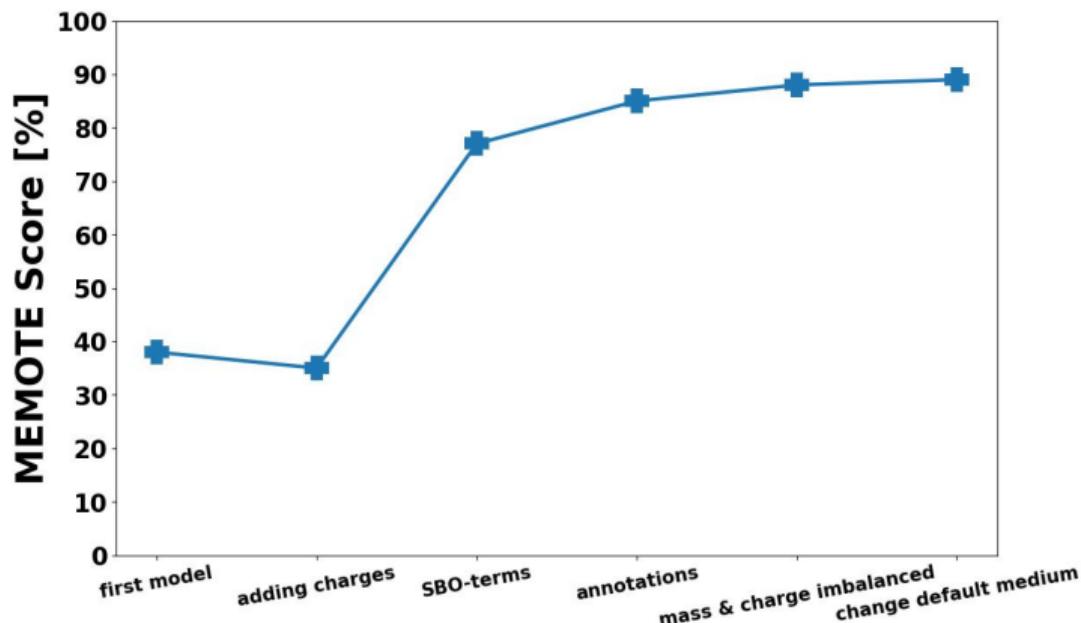
- Done with ModelPolisher
- added some outdated identifiers, which had to be removed manually

# Mass & Charge balancing



- Unbalanced reactions before curation:
  - Mass: 647
  - Charge: 35
- Unbalanced reactions after curation:
  - Mass: 41
  - Charge: 28

# Growth on SNM3



- Set SNM3 as default medium
- No initial growth:
  - Added  $Fe^{2+}$  to our medium
  - Reactions for beta-Alanine and L-Asparagine based on same reactions in *E.coli*
- Final growth rate in SNM3 +  $Fe^{2+}$ :  $0.44 \frac{mmol}{gDW \cdot h}$

# Orphan/dead-end metabolites, KEGG Pathways, Groups plugin

- Orphan & dead-end metabolites:
  - Reaction to produce pydam\_c was added based on KEGG database
- KEGG Pathways for each reaction
  - added with the KEGG API as CV Terms for each reaction
- Groups plugin
  - Groups were used as a collection of pathways
  - 98 pathways were added
  - all reactions of one pathway were added as a member
- This step caused no change in the MEMOTE score

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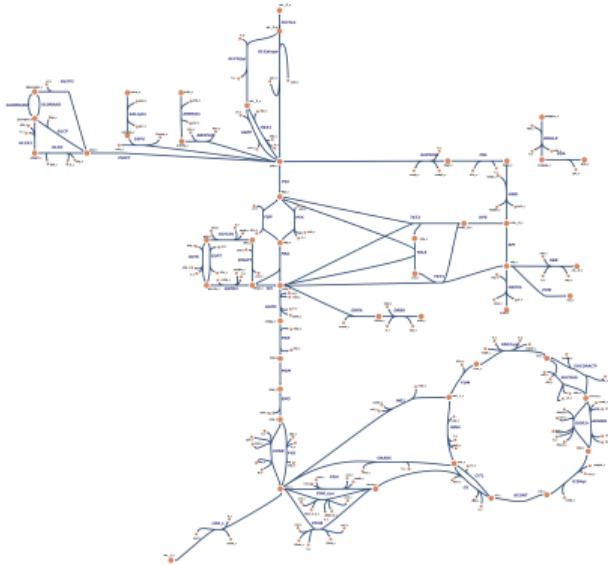
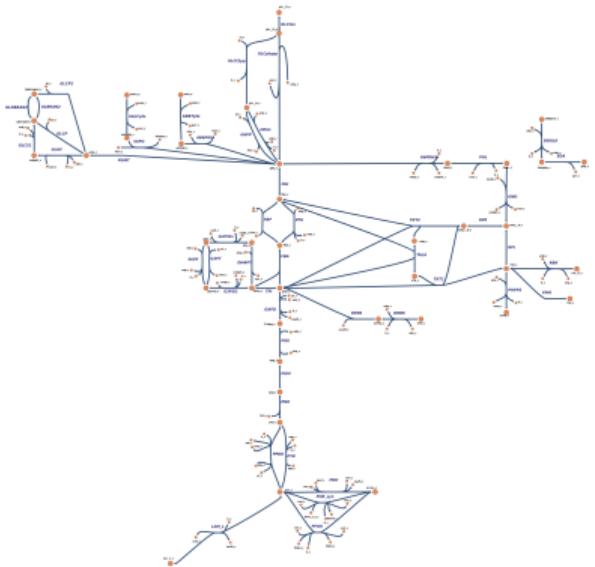
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# Example Pathway Map

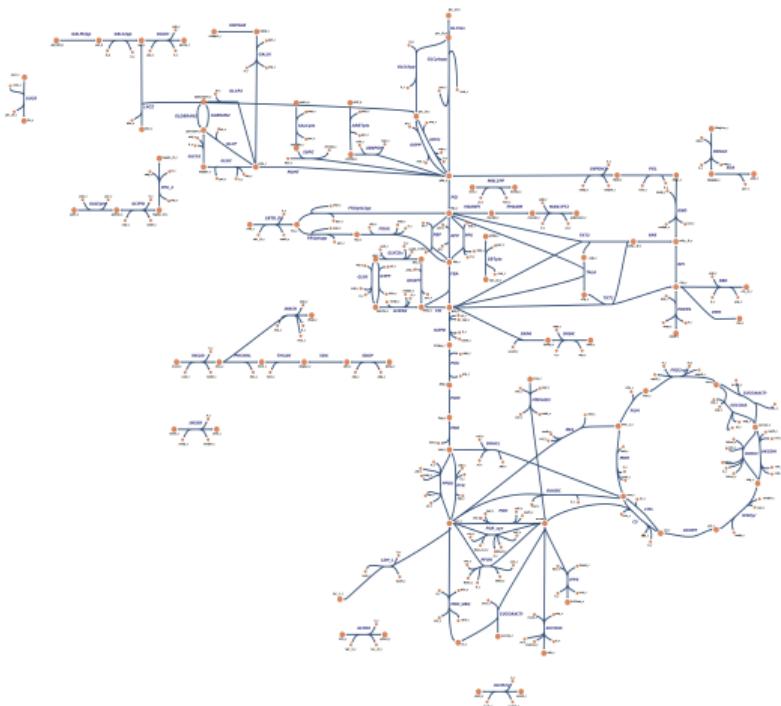
Glycolysis & Pentose Phosphate Pathway



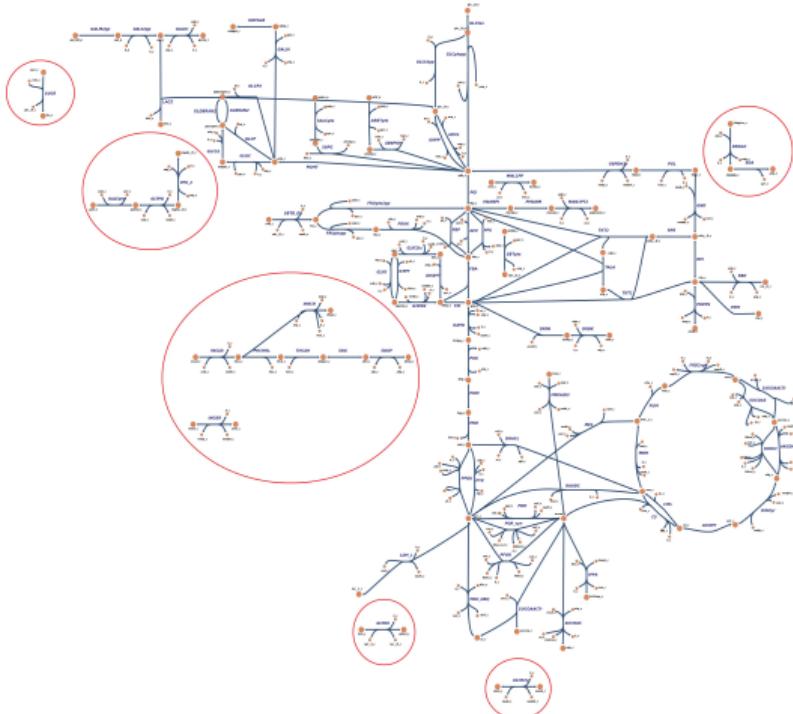
extended by TCA



# Final Map



# Final Map



- Unconnected reactions:
  - No reference for the connecting reaction in KEGG
  - Often connectable within our model

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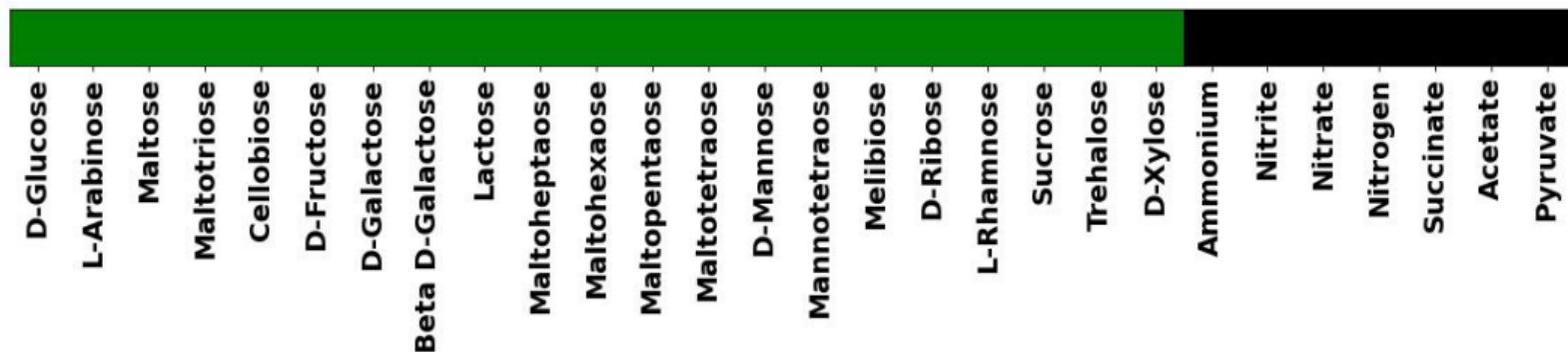
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# Model analysis

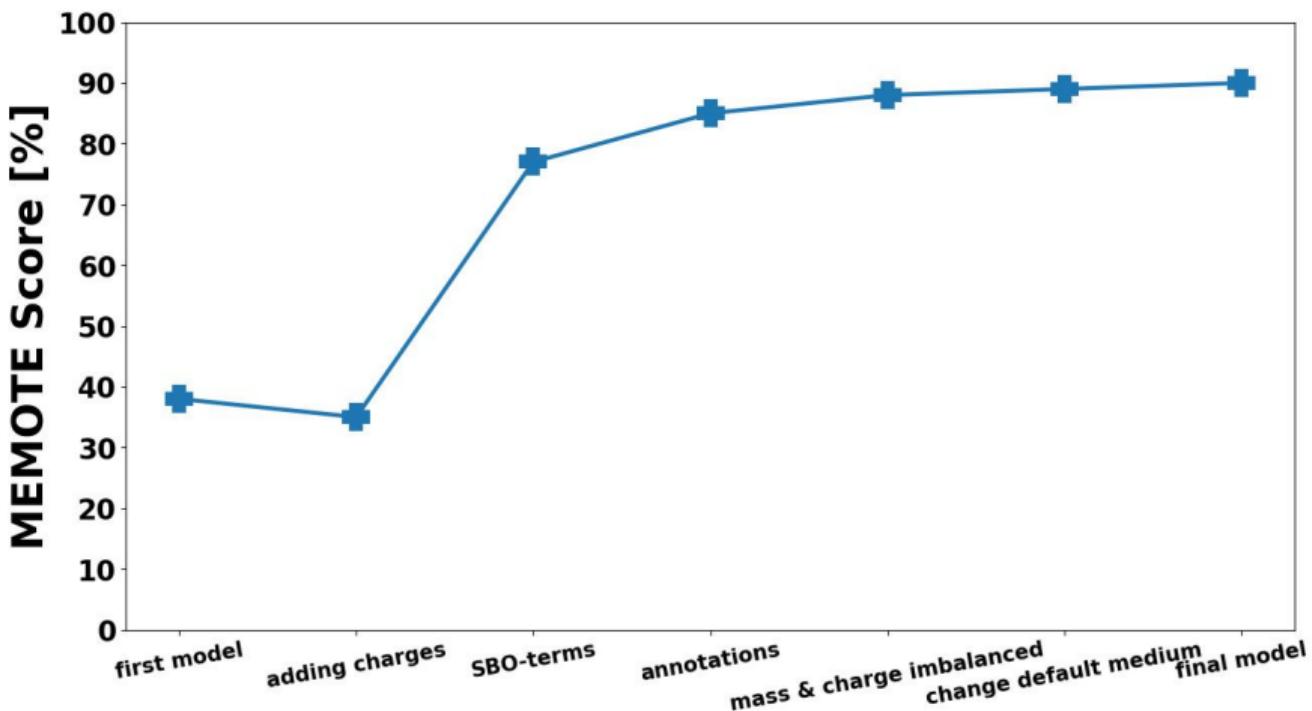
- Growth for different carbon sources

- Glucose and Fructose increased the growth rate to 12.6  $\frac{mmol}{gDW \cdot h}$  (minimal medium: 10.0  $\frac{mmol}{gDW \cdot h}$ )
- Succinate, Acetate, Pyruvate did not change the growth rate

- Growth capabilities



# Final MEMOTE report



## References

Dräger. Lecture02 Systems Biology I, Nov 2021.

Elan Medical Skin Clinic LTD. Pathogenesis of acne - Elan Medical Skin Clinic LTD, Jan 2022. URL <http://www.elan-medical-clinic.co.uk/blog/adult-acne-why-me/pathogenesis-of-acne>. [Online; accessed 31. Jan. 2022].

pcds.org.uk. acne\_polimorfo\_hirsutismo01\_2615addf7111d83624b7a7a5f3466fb3.jpg (JPEG Image, 300 × 300 pixels), Jan 2022. URL [https://www.pcds.org.uk/imager/gallery/clinical/acne-vulgaris/14350/acne\\_polimorfo\\_hirsutismo01\\_2615addf7111d83624b7a7a5f3466fb3.jpg](https://www.pcds.org.uk/imager/gallery/clinical/acne-vulgaris/14350/acne_polimorfo_hirsutismo01_2615addf7111d83624b7a7a5f3466fb3.jpg). [Online; accessed 31. Jan. 2022].

Sunhyo Ryu, Hyo Mi Han, Peter I. Song, Cheryl A. Armstrong, and Yoonkyung Park. Suppression of Propionibacterium acnes Infection and the Associated Inflammatory Response by the Antimicrobial Peptide P5 in Mice. *PLoS One*, 10(7):e0132619, Jul 2015. ISSN 1932-6203. doi: 10.1371/journal.pone.0132619.

Sebaceous gland - Wikipedia. Sebaceous gland - Wikipedia, Dec 2021. URL

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