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Artificial Metabolic Networks:
Hybrid models enabling neural computations with metabolic networks

Team BioRetroSynth

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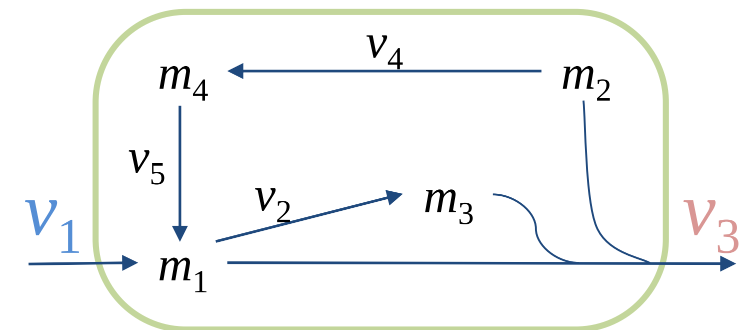
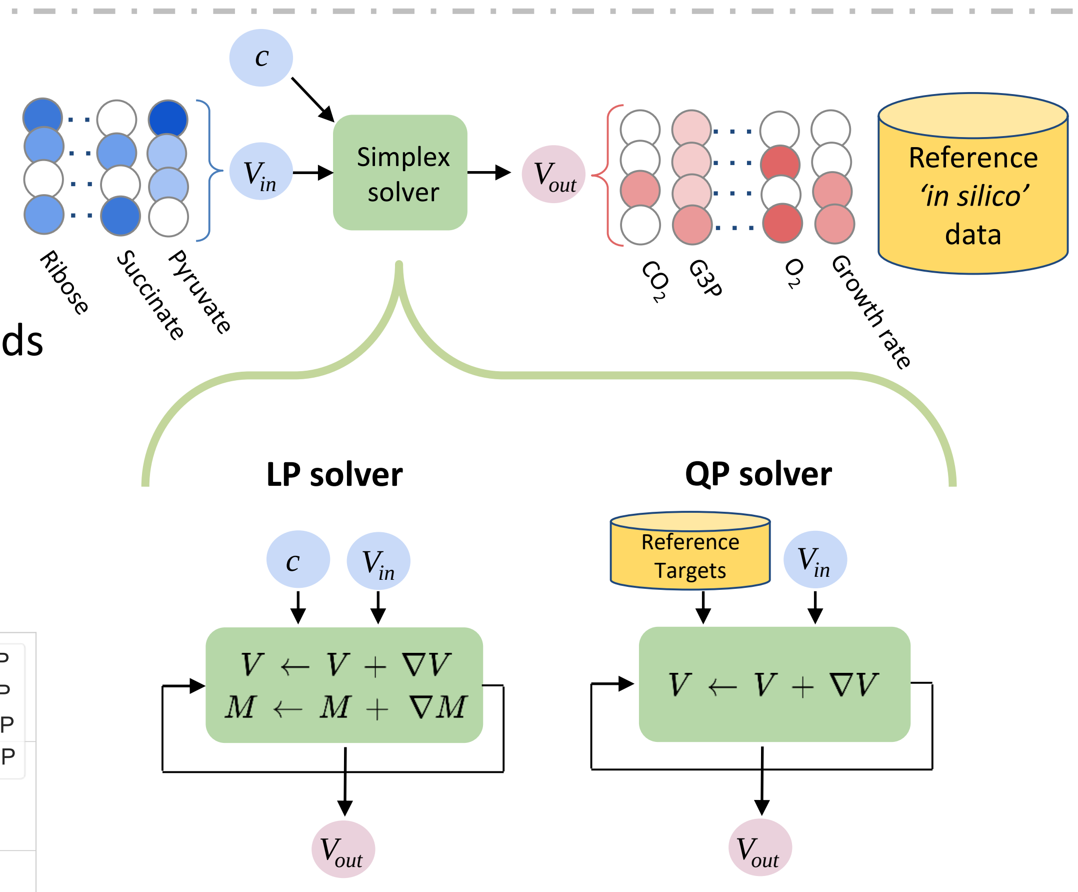
Introduction

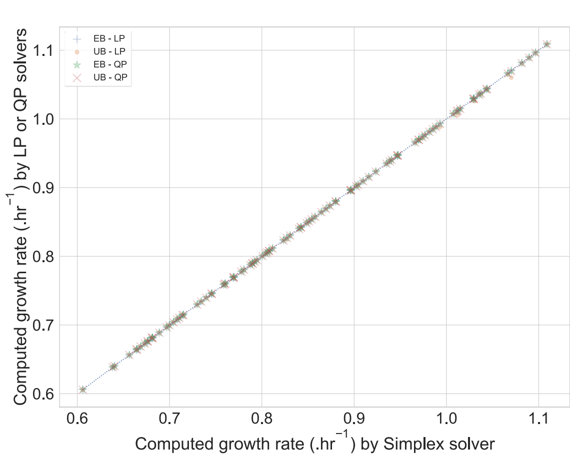
- Flux Balance Analysis (FBA): main approach for studying metabolic networks[1]
- Constrained optimization principle: with v_1 constrained, optimize v_3
- How can we surpass uptake flux measurement?

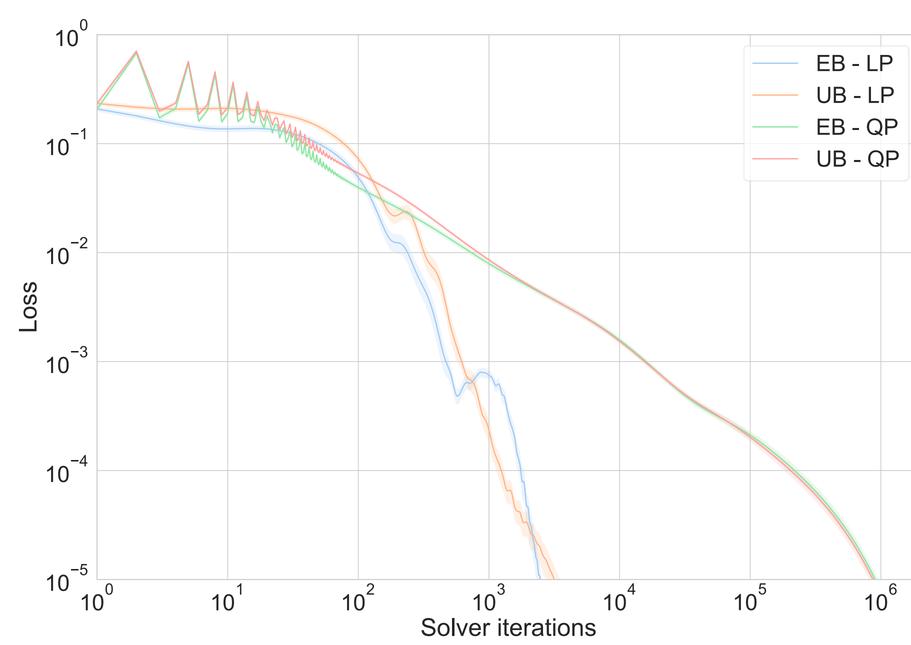


Surrogating FBA with neural methods

- Hybrid model: neural layer + mechanistic layer[2]
- Challenge: mechanistic layer compatible with gradient back-propagation
- Alternative to Simplex solver: Linear and Quadratic programming neural methods
- Custom loss function to assess constraints
- LP needs less iterations than QP
- Both perform FBA with gradient back-propagation compatibility



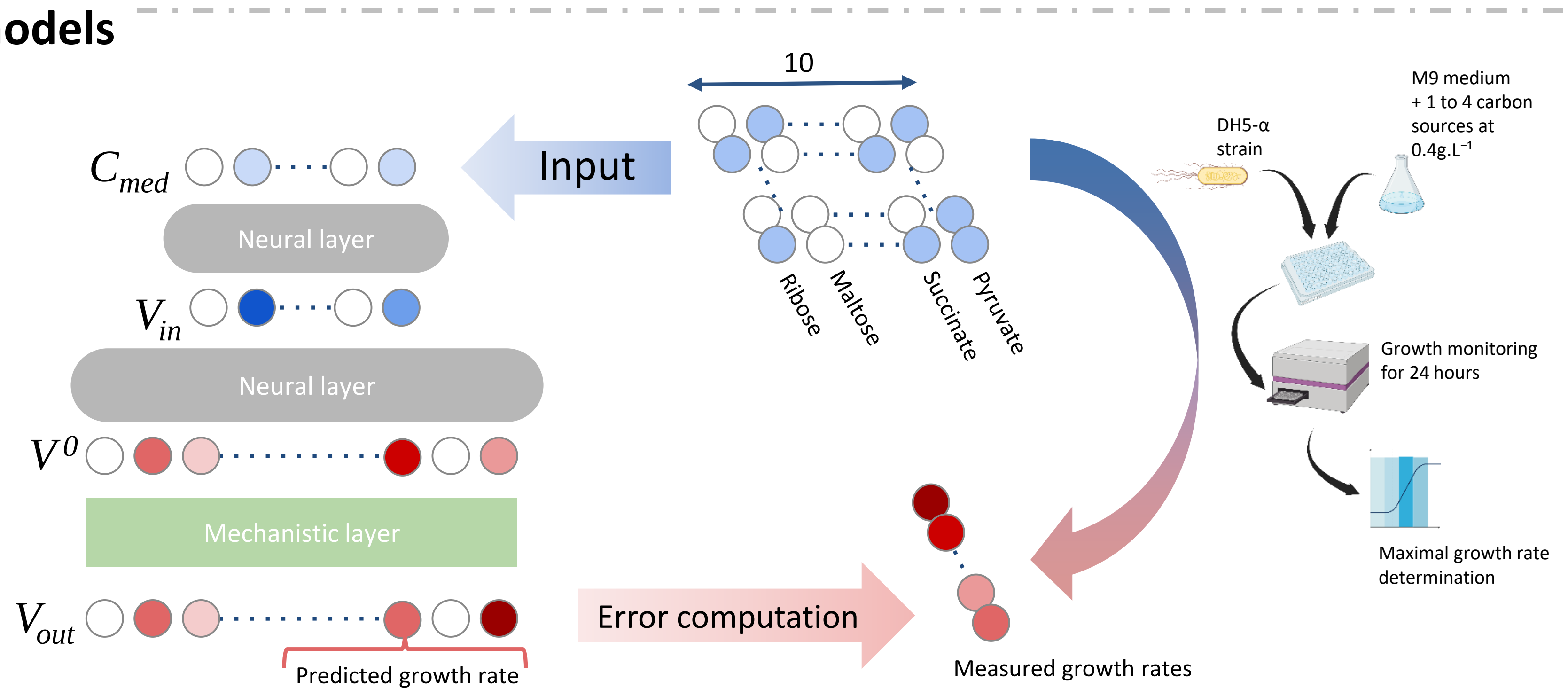


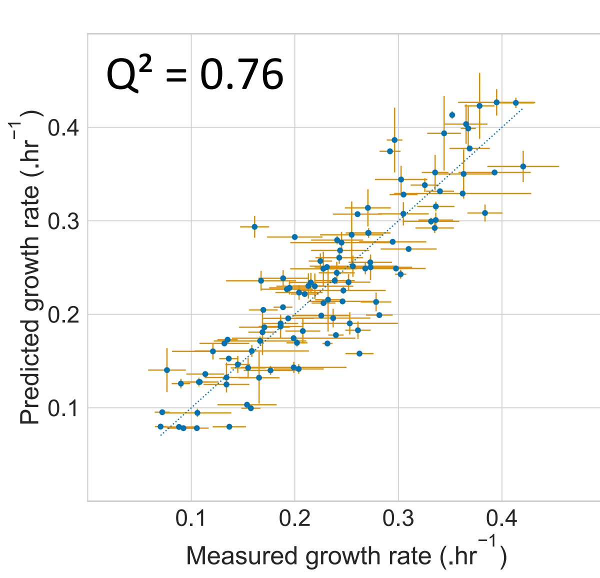


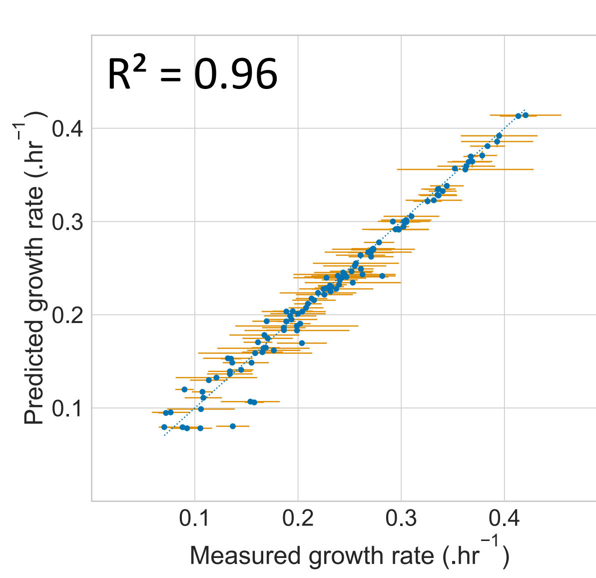
$$\mathrm{Loss} = \underbrace{\frac{1}{n_{ref}} \left\| P_{ref}V - V_{\mathrm{ref}} \right\|^2}_{\text{Reference Fluxes}} + \underbrace{\frac{1}{m} \|SV\|^2}_{\text{Mass-balance (Sv=0)}} + \underbrace{\frac{1}{n_{in}} \|ReLU(P_{in}V - V_{in})\|^2}_{\text{Uptake fluxes bounds}} + \underbrace{\frac{1}{n} \|ReLU(-V)\|^2}_{\text{Flux positivity}}$$

Learning on experimental data with hybrid models

- C_{med} describes medium concentrations
- V^0 accelerates the mechanistic layer
- Error computation: experimental growth rate + network constraints
- Backpropagation to both neural layers







Conclusions

- Successful embedding of metabolic networks in machine learning architectures
- Hybrid modelling augments mechanistic models, saving time and resources
- Opens a new door for exploiting metabolic networks

Centre
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