PyCoMo: a python package for community metabolic model creation and analysis

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Introduction

- Most organisms in nature form communities with other taxa, gaining emergent properties. Communities are of interest to many fields, including ecology, medicine and biotechnology.

- Metabolic modelling is applied to communities to gain mechanistic insights. For this, compartmentalised community metabolic models are built from individual metabolic models of their members.

- The process of building compartmentalised metabolic models includes many technical challenges, such as matching exchange metabolites across the different member models and creating a common biomass function.

- Moreover, to make the final metabolic model reusable for different analysis parameters, it is important to maintain species specific information, e.g. which genes and reactions belong to which organism, as well as the original flux bounds.

Results

PyCoMo creates Community Metabolic Models with variable growth rate or variable abundance profile and calculates possible interactions
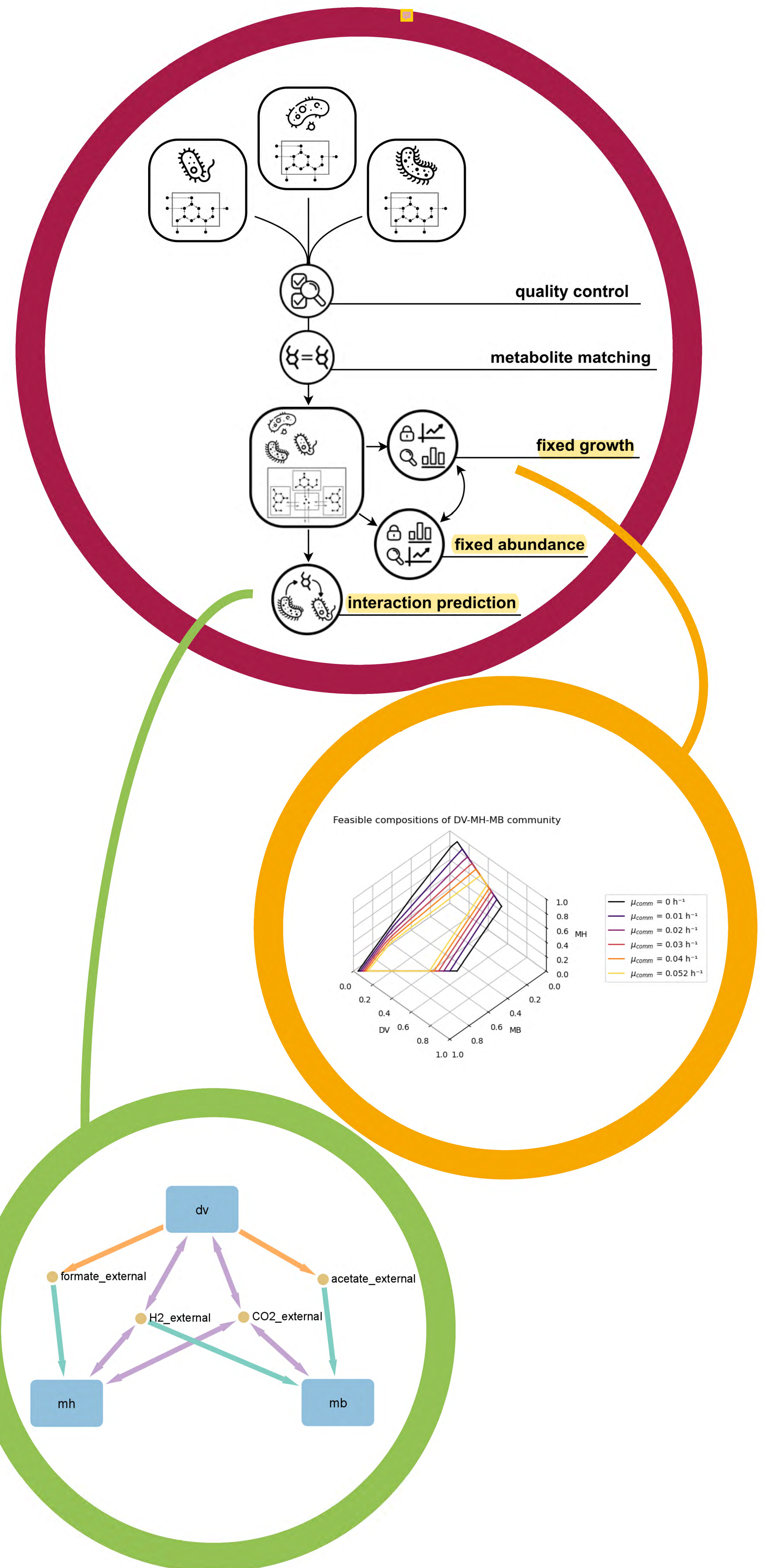
- We developed PyCoMo, a Python 3 package for the generation and analysis of compartmentalized community metabolic models. It includes quality checks on the mass balance of all reactions and matched exchange metabolites, as well as the detection of reactions that can carry flux without metabolite input in the model.

- PyCoMo can use any metabolic models and formats supported by COBRApy as input and resulting community metabolic models fully support the SBML format. The created community metabolic models retain the original flux bounds and the member of origin for all metabolites, reactions, genes and compartments.

- PyCoMo allows simulations with fixed community abundance profiles for finding the maximum/minimum flux of a reaction, e.g. the biomass function. It also supports simulations with a fixed growth rate but variable abundance profiles, allowing the search for all viable community compositions. Lastly, PyCoMo can be used to calculate the set of possible metabolite exchanges and interactions, independent of growth rate and abundance profile.

Usage example

- We show the functionalities of PyCoMo by applying it to a simplified biogas community of three species. The community consist of *Desulfovibrio vulgaris*, *Methanospirillum hungatei* and *Methanosarcina barkeri*, each representing a functional guild in the metabolic model. The models and their analysis were taken from published literature (Koch et al. 2019).

- Analysis of the community metabolic model generated by PyCoMo replicated the findings of the original study: the maximum growth rate of the community lies at 0.052 h^{-1} and all feasible compositions require the presence of *D. vulgaris*, while the presence of only one of *M. hungatei* and *M. barkeri* is required.

- A visualisation of the community and its cross-fed metabolites generated with ScyNet is shown in the bottom circle of figure 1. The network is contextualised with the possible reaction directionalities as calculated by PyCoMo. The network clearly shows food web of the community, with *D. vulgaris* supplying formate to *M. hungatei*, acetate to *M. barkeri* and H2 and CO2 to both.

Conclusion

- PyCoMo is suited for applications in large communities. We have tested PyCoMo on communities of increasing size using genome-scale metabolic models of the AGORA collection as input. In this setup, the generation of a genome-scale community metabolic model with 40 members required less than 10 minutes.

- (Manual) curation is an important part in the creation of high quality metabolic models. PyCoMo facilitates this process by retaining all information of the members' models, as well as allowing to switch between model structures of fixed growth and fixed abundance. This allows comparison of model predictions and experimental measurements on community level.

quality control

metabolite matching

fixed growth

fixed abundance

interaction prediction

Feasible compositions of DV-MH-MB community

- μ_{comm} = 0 h^{-1}
- μ_{comm} = 0.01 h^{-1}
- μ_{comm} = 0.02 h^{-1}
- μ_{comm} = 0.03 h^{-1}
- μ_{comm} = 0.04 h^{-1}
- μ_{comm} = 0.052 h^{-1}

Try it yourself!
Get PyCoMo on GitHub:

References

[1] Koch, S. *et al.* RedCom: A strategy for reduced metabolic modeling of complex microbial communities and its application for analyzing experimental datasets from anaerobic digestion. *PLoS Computational Biology* **15**, (2019).

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ScyNet: Visualizing interactions in communities with metabolic models

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Introduction

- Interactions play an important role shaping the structure and properties of microbial communities.

- Metabolic modelling has been applied to diverse communities to predict interspecies interactions. Metabolic models of communities are big and complex, with thousands of reactions and metabolites per organism at genome scale.

- Visualisation of community metabolic models helps communicating results and getting an overview of the models. Due to the complexity of the networks, visualisations need to be reduced to be informative.

- Existing reduction methods were developed for single species metabolic models and do not capture the bigger picture in communities. A reduction of the network to community members and exchange metabolites could be a suitable method for community metabolic models

Results

Community metabolic models can be visualized effectively by hiding internal metabolites and reactions

- We developed ScyNet, a community metabolic model visualisation and reduction tool for Cytoscape. The input for ScyNet are community metabolic models in SBML file format. Models with the required format can be easily generated from the members' metabolic models using PyCoMo.

- The size of community metabolic networks is **reduced** by combining all internal fluxes into a single node per community member.

- ScyNet can be used to **contextualize** the visualisation with flux data (flux values or ranges). This approach can also be used for custom coloring of the edges. The color scheme was selected to be color-blind friendly.

- A layout algorithm was developed for hierarchically structuring the reduced network.

- ScyNet can further **focus** the network to cross-feeding interactions.

Usage example

- The procedure of ScyNet is shown with an example community metabolic model analysed by Henson et al. It is a cystic fibrosis airways community with 4 members. Each member is a representative of their phylum, with the four included phyla being the most abundant in the dataset of Henson et al.

- The metabolic models of the community members are part of the AGORA collection (version 1). The metabolic models were combined into a compartmentalized community metabolic model with PyCoMo.

- The community metabolic model consists of 4787 metabolites and 5636 reactions, shown in the top circle of figure 1. A reduction of the network with ScyNet decreases the size to 234 metabolites and 565 reactions.

- The network was contextualized with the results of flux balance analysis (FBA) with fixed community composition (0.25 for each community member). A final network reduction with a focus on the cross-fed metabolites, and removal of the metabolites H_2O and H^+, yields a network with 6 metabolites and 20 reactions.

Conclusion

- The development of ScyNet started as part of a software development project by Kilian Gandolf and Michael Hofer.

- ScyNet was tested on communities of up to 17 members. Larger communities also result in more exchanged and cross-fed metabolites, increasing the size of the networks produced by ScyNet. For informative visualisations of larger communities requires further reduction methods like modularisation, which could be added to ScyNet.

- The compute time for the usage example was less than 5 minutes. This not only includes the time needed for network reduction, contextualisation and visualisation, but also the generation of the community metabolic model, starting with only the individual metabolic models of the community members.

Reduce

Contextualize

Focus

Try it yourself!
Get ScyNet on GitHub:

References

[1] Henson, M. A., Orazi, G., Phalak, P. & O'Toole, G. A. Metabolic Modeling of Cystic Fibrosis Airway Communities Predicts Mechanisms of Pathogen Dominance. *mSystems* **4**, e00026-19 (2019).

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