155. Modeling metabolic dynamics in 3D: applications to synthetic microbial ecosystems

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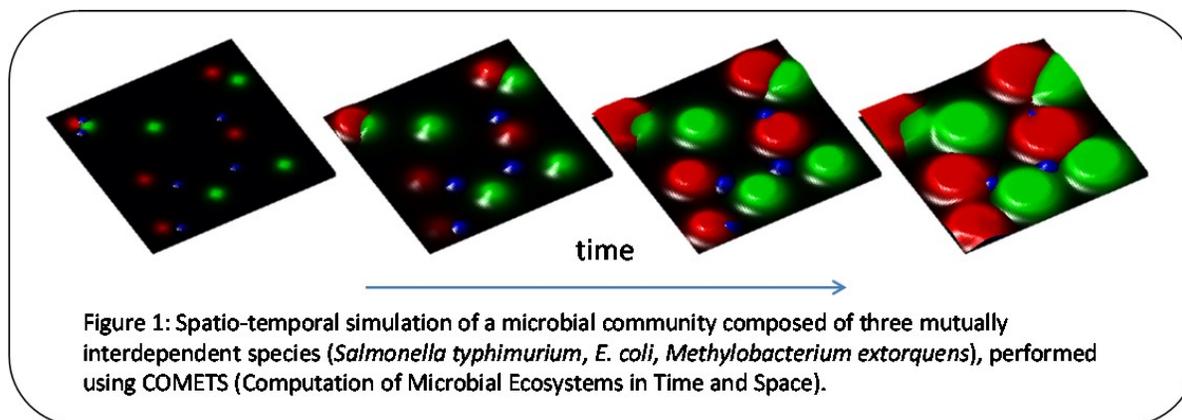
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Project goals: The goal of this project is to develop and test a computational tool for modeling metabolic flux and inter-species interactions in spatially structured microbial ecosystems. Our approach, named Computation of Microbial Ecosystems in Time and Space (COMETS), combines dynamic flux balance modeling with diffusion. Experimental testing has confirmed the capacity of COMETS to predict nontrivial results about the spatio-temporal dynamics of small synthetic communities. Our initial 2D version is being expanded to a 3D version, and applied to a systematic large-scale study of pairwise interactions between microbes relevant to biofuel production, bioremediation and biogeochemical cycles.

Although often studied alone in well-mixed flasks, most microbial organisms live in multi- species, structured, highly dynamic consortia [1]. COMETS is a multi-scale modeling framework that computes ecosystem-level metabolic dynamics based on detailed intracellular metabolic stoichiometry, without any a priori assumption on whether and how different species would interact. It implements a dynamic FBA (dFBA, [2]) algorithm on a lattice, making it possible to track the spatio-temporal dynamics of multiple microbial species in complex environments with complete genome scale resolution [3]. As a first test of COMETS we verified that it can quantitatively recapitulate known aspects of single colony growth, such as the linear expansion of colony diameter, under different carbon sources. We than applied COMETS to a previously constructed *E. coli*/*S. enterica* artificial consortium [4], and showed that the simulation correctly predicts the convergence of the system to specific species ratios. More surprisingly, COMETS yielded correct predictions also for a newly engineered three-member consortium that incorporates *Methylobacterium extorquens* AM1 into the *E. coli*/*S. enterica* system (Figure 1). Finally, we investigated the impact that spatial arrangement has on colony interactions, with special attention to a puzzling shadowing effect between colonies that engage in syntrophic interactions, which we refer to as a "metabolic eclipse". We found that COMETS accurately predicts community interactions and dynamics as the natural outcome of intracellular metabolic processes, and suggests unexpected new features of model consortia, with important implications for understanding natural and synthetic microbial communities. From its initial two- dimensional version, COMETS has now been extended to a fully functional three dimensional platform. COMETS in 3D can find extensive applications in the detailed study of bacterial biofilm growing in structured environments and environmental gradients.

COMETS 3D visualization is based on the open source OpenGL 3D library implemented as Java binding (JOGL), thus maintaining the open source nature of the code. Additional new features being added to COMETS include the capacity to model metabolite diffusion through biomass, and the introduction of lag phase. Moreover, we have been able to import in COMETS more than a hundred stoichiometric models from Model SEED [5], paving the way for systematic combinatorial studies of inter-species interactions.

Figure 1: Spatio-temporal simulation of a microbial community composed of three mutually interdependent species (*Salmonella typhimurium, E. coli, Methylobacterium extorquens*), performed using COMETS (Computation of Microbial Ecosystems in Time and Space).

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