CHRR: Coordinate hit-and-run with rounding for uniform sampling of metabolic networks

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Project Goals: Development of a framework for mass conserved elementary kinetic modelling of metabolic networks [1, 2, 3, 4, 5]. This collaborative project was motivated by a need for data to constrain and validate metabolic models. Sampling algorithms have demonstrated applications in measurement and estimation of kinetic parameters, steady state fluxes and metabolite concentrations for biochemical systems [6, 7, 8].

In constraint-based modelling, physicochemical and biochemical constraints define a set of feasible states of a biochemical network. Steady state mass conservation and limits on substrate uptake constraints are specified by a set of linear equalities and inequalities that define a polyhedral convex set of feasible flux vectors. Uniform sampling of this set provides an unbiased characterisation of the metabolic capabilities of a biochemical network [9]. However, reliable uniform sampling of genome-scale biochemical networks is challenging due to their high dimensionality and inherent anisotropy. Here, we apply a new sampling algorithm, coordinate hit-and-run with rounding (CHRR) [**?**], to metabolic networks of increasing dimensionality. This algorithm is based upon the provably efficient hit-and-run random walk [10] and crucially, it uses a preprocessing step to round the anisotropic flux set. CHRR provably converges to a uniform stationary sampling distribution and does so several times faster than a popular artificial centering hit-and-run (ACHR) algorithm [11]. We demonstrate the effects of improved convergence rate on predictions of the metabolic capabilities of Bacillus Subtilis [12].

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