Evolution of metabolic dependencies: is gene loss enough?

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Background: Microbial ecologists have recently become interested in gaining a mechanistic understanding of how microbes become metabolically dependent either on each other or on their host organisms [1, 2, 3]. Towards this end, the bulk of recent efforts have focused on validating the Black Queen hypothesis: which states that dependencies can evolve through "adaptive gene loss" [4, 5, 6] (i.e. losing genes which are costly to an individual but provide a common good to the population). A swathe of both experimental [7, 8, 9, 10, 11, 12] and theoretical [13, 14, 15, 16, 17] studies from the past five years can now demonstrate that this is evolutionarily feasible: administering the loss of even a few "costly" genes can initiate a strong metabolic dependence in microbial consortia.

Critique: However, we believe that these studies miss two major examinations: (a) given the widespread possibility of gene acquisition (say via horizontal gene transfer [18]), are differences between known free-living genomes and known metabolically-dependent genomes actually consistent with rampant gene loss? and (b) are there other feasible evolutionary paths (as in ref. [16]) towards (hitherto unknown but possible) dependent metabolisms that require a mixture of gene loss and gain? These examinations will crucially supplement our understanding of the evolution of metabolic dependencies since contemporary studies either rely on a few specific examples that represent "extreme" atypical cases (e.g. dependent mutants with a few engineered gene deletions [7, 9] and obligate endosymbionts with severely reduced genomes [19, 20]) or simulate gene loss "by hand" to show that it suffices to generate metabolic dependencies (without examining as we state, a mixture of loss and gain).

Proposal: We propose here a simple model that accomplishes both these goals: (a) we motivate why we expect both gene loss and gain to be typical in real metabolisms. For this, we survey several real prokaryotic metabolic networks both independent and dependent; surprisingly, we find that the difference between an independent and a dependent network is often an assortment of both lost and gained genes; and (b) we study evolutionarily feasible trajectories to dependency through dynamical network modification. Here we iteratively modify independent metabolic networks through pathway addition and deletion till we arrive at a hypothetical (not yet sequenced but possible) dependent metabolism; we find that dependents often arise from pathways being added and removed in concert (reflecting a combination of gene addition and removal).

Impact: We hope that these results facilitate a rethink of how metabolic dependencies can and have emerged in naturally occurring microbial populations, especially those observed outside stable, unchanging environments like host guts.

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