Bacterial colonization of phenotypic spaces

Germán Plata, PhD & Dennis Vitkup, PhD
Department of Systems Biology, Columbia University Medical Center, New York, NY 10032
gap2118@cumc.columbia.edu

How do bacterial phenotypes change over billions of years?

Materials and methods

- Hundreds of genome-scale metabolic models
- 16S rRNA tree
- Estimate divergence (16S rRNA)
- Predict using Flux Balance Analysis (FBA):
  - Ability to use nutrients
  - Gene essentiality
  - Gene pair synthetic lethality
- Compare binary phenotypic profiles (Jaccard similarity) as a function of divergence

Decay of phenotypic similarity

- Wide diversity within closely related strains
- Exponential decay of phenotypic similarity
  \[ y = a + b \times e^{-ct} \]
- Maximum divergence within ~2 billion years

Experimental validation

- 40 species
- 62 carbon sources

Gene deletion phenotypes

- About half of essential genes remain essential
- Synthetic lethality is not conserved

Rates of phenotypic change

- Metabolic phenotypes change at a rate of ~1% per carbon source per 10 million years
- Rates deviate less than 30% across bacterial classes

Evolutionary simulation

- Lineages simulated using the Gillespie algorithm:
  Next fixed phenotype and time to fixation proportional to fixation rates:
  \[ r = \mu N_e \left( \frac{1 - s^{-2}}{1 - s^{-2} N_e} \right) \]
- Results are consistent with a constant probability that species adapt to new environments per unit time

Long-term sampling of environments

- Compared most common C-sources within clades
- Older clades converge to similar nutrient usage frequencies
- Suggests environments are equally accessible in the long-term

Conclusion

- Phenotypes change at similar constant rates
- Long-lived clades ‘fill’ phenotypic space

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