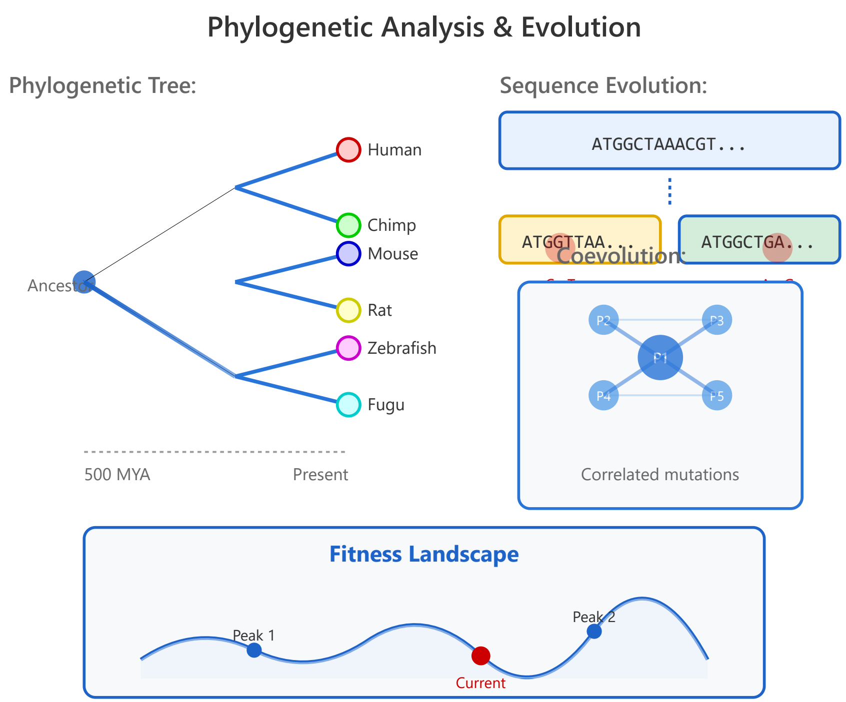
Evolution Modeling

Computational Approaches to Understanding Biological Evolution



Sequence Evolution
Substitution models & rates

Phylogenetic Inference
Tree reconstruction methods

Ancestral Reconstruction
Ancient sequence prediction

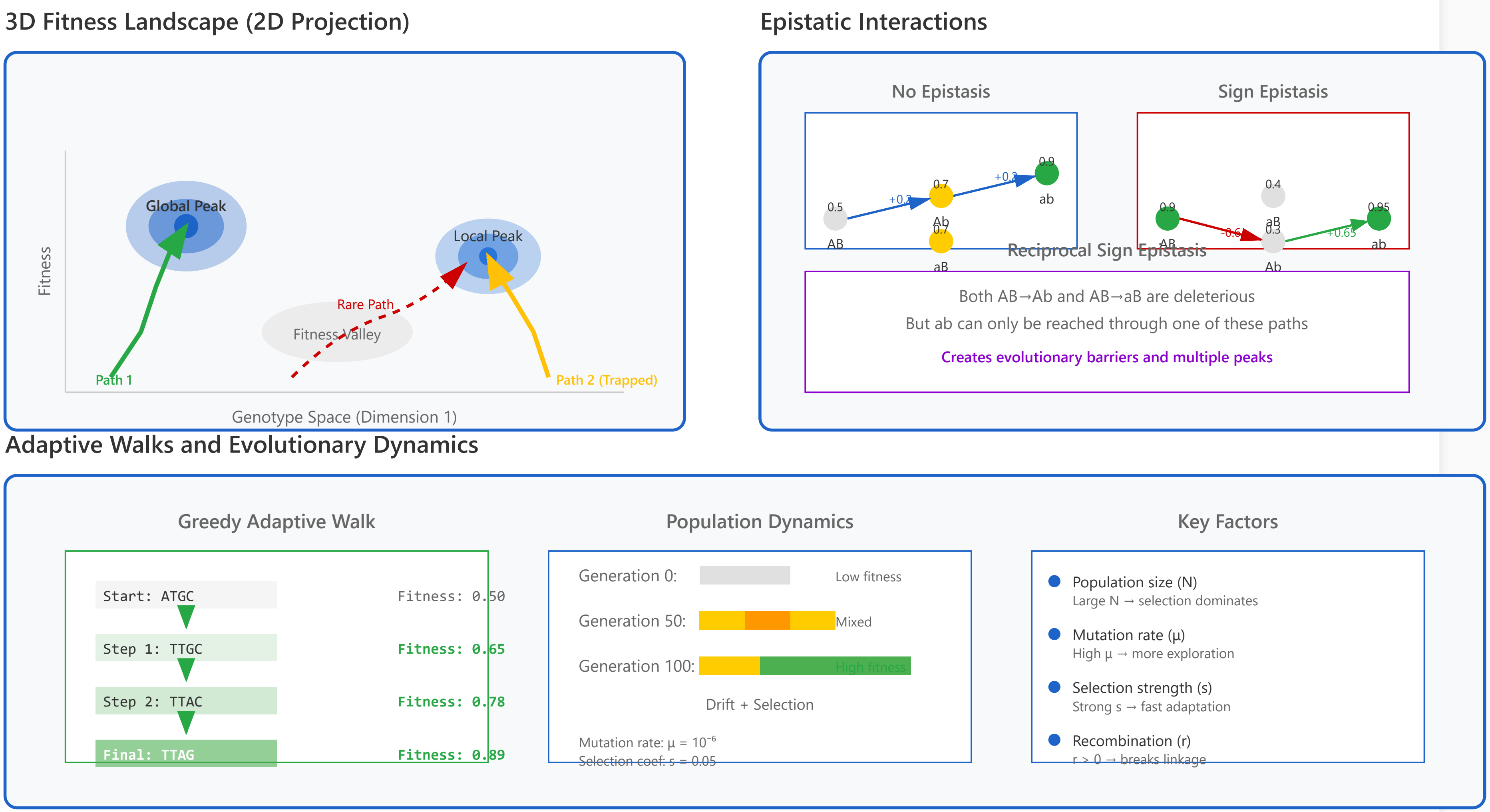
Coevolution
Correlated mutations analysis

Fitness Landscapes
Adaptive evolution mapping

5 Fitness Landscapes

Fitness landscapes represent the relationship between genotypes or phenotypes and their reproductive success. These multidimensional spaces help us understand evolutionary trajectories, constraints on adaptation, and the accessibility of beneficial mutations through the complex topology of sequence space.

Fitness Landscape Topology and Evolutionary Paths



Key Concepts:

- **Fitness Peaks:** Genotypes with maximum fitness in their local neighborhood; populations tend to evolve toward peaks
- **Fitness Valleys:** Low-fitness regions between peaks that can trap populations and prevent access to higher peaks
- **Ruggedness:** The complexity of the landscape; rugged landscapes have many local optima
- **Epistasis:** Interactions between mutations where the effect of one depends on genetic background
- **Sign Epistasis:** When a mutation is beneficial in one background but deleterious in another
- **Evolutionary Accessibility:** Which genotypes can be reached through single mutational steps
- **Adaptive Walks:** Trajectories through sequence space following fitness gradients

Wright-Fisher Model for Fixation Probability:

$$P(\text{fixation}) \approx (1 - e^{-2Ns}) / (1 - e^{-4Ns})$$

where N = population size, s = selection coefficient

Example: Antibiotic Resistance Evolution

Studies of beta-lactamase evolution revealed a rugged fitness landscape where the path to high-level antibiotic resistance requires crossing fitness valleys. Some highly resistant variants can only be accessed through specific mutational paths involving 5+ mutations, explaining why certain resistance mechanisms emerge more frequently than others in clinical settings. Sign epistasis between mutations means that intermediate genotypes have lower fitness, creating evolutionary constraints.

🧬 Protein Engineering

Navigate sequence space to design proteins with desired properties

💊 Drug Resistance

Predict evolutionary trajectories of pathogens under drug pressure

🌱 Crop Improvement

Guide breeding strategies to optimize multiple traits simultaneously

🧫 Synthetic Biology

Design genetic circuits with predictable evolutionary stability