Neutralism

Motoo Kimura


Neutral Theory of Molecular Evolution

Motivated by problem of "mutational load": reduction in population mean fitness (relative to maximal fitness) due to mutation accumulation if all mutations are visible to selection

Asserted that calculated substitution rates would produce an unsustainably high mutational load unless the most substitutions are selectively neutral.

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Kimura and Ohta 1974: Principles

1. Rate of amino acid substitution at a protein is constant as long as mutations don’t affect protein function
2. Functionally less important parts of a molecule evolve faster
3. Substitutions that don’t disrupt the function of a molecule occur more frequently
4. Gene duplication must precede the emergence of a gene having a new function.
5. Selective elimination of deleterious mutants and random fixation of selectively (nearly) neutral mutants occur far more frequently than positive selection on advantageous mutants

Neutralist-selectionist debate

Neutralism: most fixation events due to drift of (nearly) neutral mutations

Neo-darwinism: merging of Darwinian and Mendelian theory - gave central role to selection in evolution

Pan-selectionism: extreme reliance on selection as evolutionary explanation:
  - Fixation events due to positive selection
  - Polymorphisms due to balancing selection
The neutralist position

Neutralism: most fixation events due to drift of (nearly) neutral mutations
Under “neutralism” selection can still act, but $|s|$ must be less than $1/(2Ne)$
Substitution and polymorphism are trails of the same process (drift)
Polymorphisms are unstable and transient
Adaptation can even occur without positive selection (purging of deleterious alleles)

The selectionist position

Pan-selectionism: extreme reliance on selection as evolutionary explanation:
- Fixation events due to positive selection
- Polymorphisms due to balancing selection
Substitution and polymorphism are evidence of different types of selection (positive and balancing, respectively)
Polymorphism is generally stable and adaptive.

Neutralist-selectionist debate

Dispute centers on role of drift vs selection
Also on the fitness of new mutations
Both agree that many new mutations are deleterious
But are the rest neutral or not?

“...roars of "The Neutral Theory Is Dead" and "Long Live the Neutral Theory" will continue to reverberate, sometimes in the title of a single article...”