The Origin of Gene Subfunctions and Genotypic Complexity by Modular Restructuring

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Subdivision and specialization - a trend in evolution

Evolutionary Time
Is the Increasing Phenotypic Specialization Reflected in Underlying Genetic Circuitry?
What is the default contribution to specialization of body regions at the genotypic level produced by mutation pressure and genetic drift?
• Modular Restructuring

Evolution of differential connectivity of the genotypic-phenotypic map via \textit{subfunction formation} and \textit{resolution} in developmental genetic networks by nearly neutral processes
• Modular Restructuring

  Evolution of differential connectivity of the genotypic-phenotypic map via *subfunction formation* and *resolution* in developmental genetic networks by nearly neutral processes

• Subfunction Formation

  The processes which lead to origin of new gene subfunctions either by co-option or fission mechanisms
• Modular Restructuring

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• Subfunction Formation

  The processes which lead to origin of new gene subfunctions either by co-option or fission mechanisms

• Subfunction Resolution

  The processes which lead to the partitioning of existing subfunctions between gene duplicates by DDC mechanisms
Multifunctional gene

Subfunction 1

Subfunction 2
Given that many genes are multifunctional, how do new subfunctions evolve?
Subfunction Co-option
Subfunction Fission
TFA and TFB

TFA and TFC

TFA and TFB

TFA and TFC
TFA and TFB

TFA and TFC

B A

TFA

TFB

TFC
Fission Phase 1: Accretion, Degeneration, and Replacement
\[ P_{XW} = \left(\frac{1}{2\mu_a} + 4N_e\right)^{-1} \quad P_{YX} = \left(\frac{1}{\mu_a} + 4N_e\right)^{-1} \quad P_{ZY} = \left(\frac{1}{\mu_d} + 4N_e\right)^{-1} \]

State W (Abc)

State X (AbC) or (ABc)

State Y (ABC)

State Z (aBC)

\[ P_{WX} = \left(\frac{1}{\mu_d} + 4N_e\right)^{-1} \quad P_{XY} = \left(\frac{1}{2\mu_d} + 4N_e\right)^{-1} \]
Time for subfunction fission phase 1 when the addition and deletion rates are equal
When the time to fission for phase 1 is very long in large effective population sizes does this mean the precursor allele (ABC allele) is unavailable?
Infinite population size equilibrium frequencies for the 3 site fission model.
The effect of population size on the equilibrium frequencies under the 3 site fission model.
What about multiple TF binding Sites?

AABBCC
Effects of additional TF binding sites on the time to fission phase 1 under the 6 site model.
More complex models have similar behavior to that of the basic 3-site model

1) Increasing the number of TF binding sites in the 6-site model does not significantly change the behavior relative to the 3-site model, but does reduce the time for phase 1

2) Allowing for different rates of mutation of the A site relative to the B and C sites does not significantly change the behavior of 3 site model for reasonable mutation rates
The probability of enhancer subfunctionalization

Pr(Enhancer Subfunctionalization)

Effective Population Size

Ratio1=.25
Ratio2=.75
Ratio1 est 1
Ratio1 est 2
Ratio2 est 1
Ratio2 est 2
Modular Restructuring

1) Subfunction Fission and Modularization

2) Subfunction Resolution between Duplicate Genes

3) Genetic Network Resolution and Phenotypic Diversification
Summary:

Subfunction fission leads to the emergence of new subfunctions from the splitting of old subfunctions and may proceed under the guidance of mutation pressure in small populations ($N\mu < .1$).

More generally, small effective population size and mutation may be sufficient to drive the evolution of the complexity of genes, networks, and developmental pathways passively by modular restructuring.

Changes in the underlying genetic architecture may not be initially observed at the phenotypic level. However, the long-term cumulative effects of modular restructuring may lead to abrupt and rapid changes at the phenotypic level when organisms find themselves exposed to novel environments.
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