Molecular signatures of selection

- Because synonymous substitutions do not alter the protein, we often <u>posit</u> that they are neutral

- The **rate** of accumulation of synonymous substitutions (**dS**) can serve as the neutral background evolutionary rate

- We can compare the **rate** of accumulation of non-synonymous substitutions (**dN**), which alter the protein sequence, to **dS** and use their ratio to classify the nature of the evolutionary process

$$dS \sim \frac{\text{number of fixed synonymous mutations}}{\text{proportion of random mutations that are synonymous}}$$

$$dN \sim \frac{\text{number of fixed non-synonymous mutations}}{\text{proportion of random mutations that are non-synonymous}}$$

What can the denominator proportions depend on?

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$$dS \sim \frac{\text{number of fixed {\color{green} synonymous} mutations}}{\text{proportion of random mutations that are {\color{green} synonymous}}}$$

$$dN \sim \frac{\text{number of fixed {\color{red} non-synonymous} mutations}}{\text{proportion of random mutations that are {\color{red} non-synonymous}}}$$

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Evolutionary Modes

Positive Selection (Diversifying)	dS < dN or $\omega := dN/dS > 1$
Negative Selection	dS > dN or $\omega < 1$
Neutral Evolution	dS ≃ dN or $\omega ≃ 1$