Diversification:
an antigenic site in H3N2 IAV hemagglutinin

Nucleotides

Amino acids

36
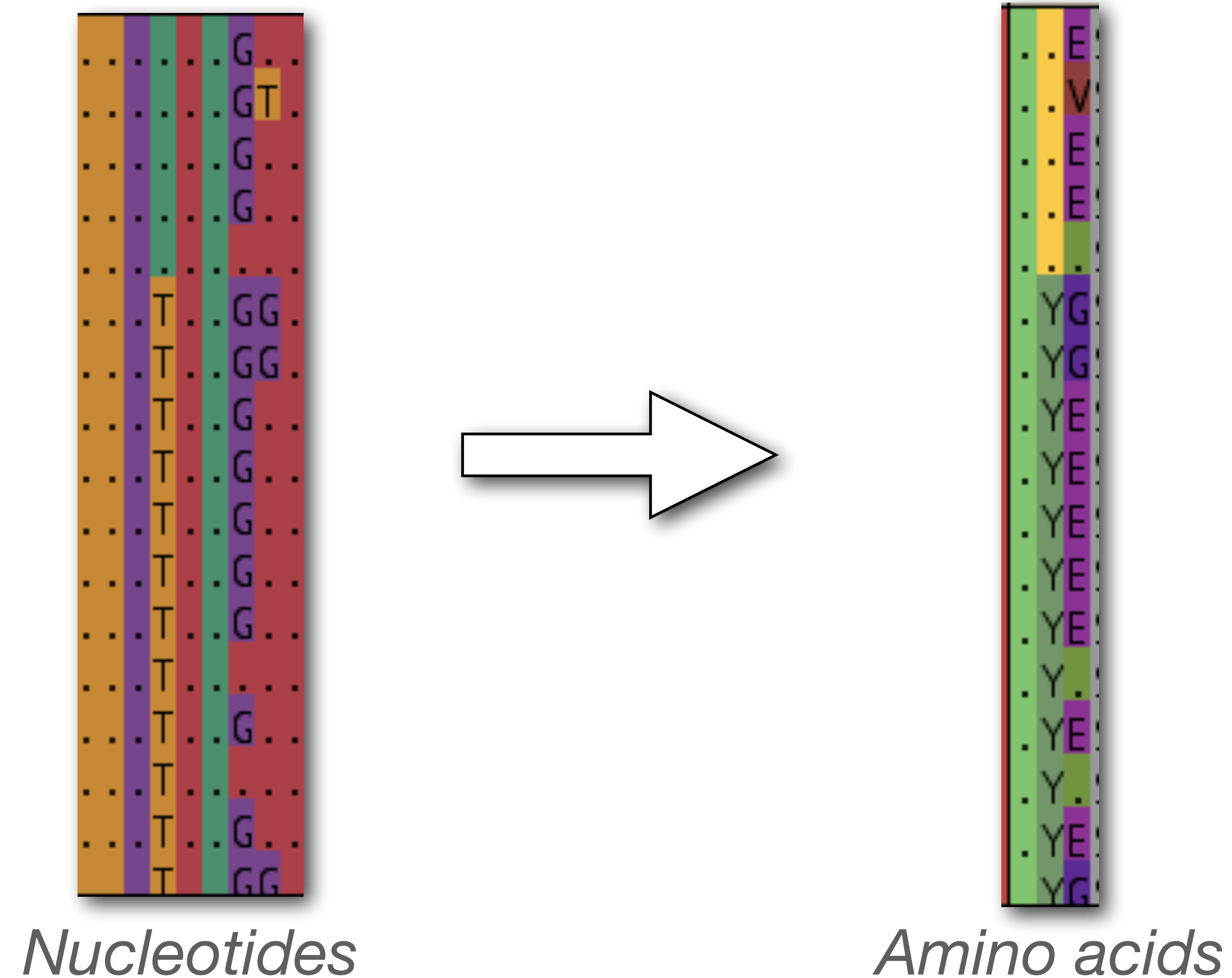
Molecular signatures of selection

- **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

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

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