

A

cells or viruses carrying codon mutants of gene; frequency of codon x at site r is $\mu_{r,x}$



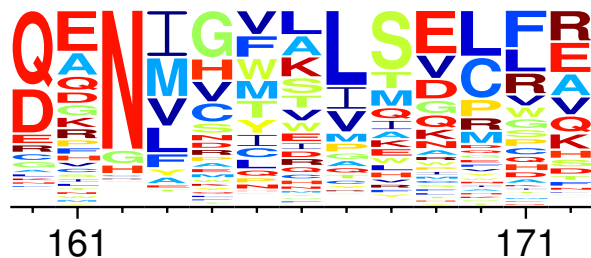
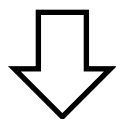
atg CAT atc ...
TtC gct atc ...
atg gct aCG ...
atg gTt atc ...
atg CCA atc ...

functional selection

cells or viruses after selection for gene function; frequency of x at r is $f_{r,x}$



atg gct aCG ...
atg gct aCG ...
atg CCA atc ...
atg CCA atc ...
atg CAT atc ...

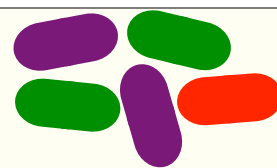


Data are analyzed to infer the preference of each site for each amino acid. This example shows a strong preference for N at site 162, and a preference for hydrophobic amino acids at sites 163 and 167.

B

control selection

new selection (e.g. drug)



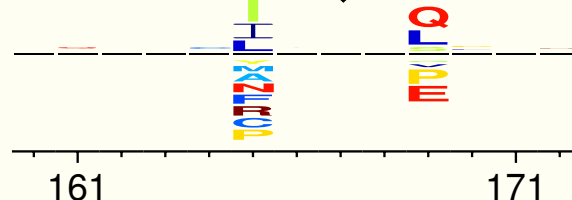
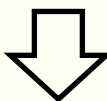
atg gct aCG ...
atg gct aCG ...
atg CCA atc ...
atg CCA atc ...
atg CAT atc ...

cells or viruses after control selection ($s1$) to maintain function; frequency of x at r is $f_{r,x}^{s1}$



atg gct aCG ...
atg CCA atc ...
atg CAT atc ...
atg CAT atc ...
atg CAT atc ...

cells or viruses after selection ($s2$) in new condition; frequency of x at r is $f_{r,x}^{s2}$



Differential preferences represent changes in selection. In this example, selection $s2$ favors T at site 165, and Q or L at site 169.