

# Rate matrix for an MG-style codon model

$$(\text{Rate})_{X,Y}(dt) = \begin{cases} \alpha & \pi_t dt & , \text{ one-step, synonymous substitution,} \\ \beta & \pi_t dt & , \text{ one-step, non-synonymous substitution,} \\ 0 & & , \text{ multi-step.} \end{cases}$$

$X, Y = \text{AAA...TTT}$  (excluding stop codons),  
 $\pi_t$  - frequency of the target nucleotide.

Example substitutions:

AAC → AAT (one step, synonymous - Asparagine)

CAC → GAC (one step, non-synonymous - Histidine to Aspartic Acid)

AAC → GTC (multi-step).

$\alpha R_{CT}$   
 $\beta R_{CG}$

$\alpha$  (syn. rate) and  $\beta$  (non-syn. rate) are the key quantities for all selection analyses

# Computing the transition probabilities

- In order to recover transition probabilities  $\mathbf{T}(t)$  from the rate matrix  $\mathbf{Q}$ , one computes the matrix exponential  $\mathbf{T}(t) = \exp(\mathbf{Q}t)$ , same as with standard nucleotide models, e.g. HKY85 or GTR.
- Because the computational complexity of matrix exponentiation scales as the cube of the matrix dimension, codon based models require roughly  $(61/4)^3 \approx 3500$  more operations than nucleotide models.
- This explains why codon probabilistic models were not introduced until the 1990s, even though they are relatively straightforward extensions of 4x4 nucleotide models