Computing the transition probabilities

- In order to recover transition probabilities **T(t)** from the rate matrix **Q**, one computes the matrix exponential **T(t)** = **exp(Qt)**, 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 ≈ 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

Multiple substitutions

- The model assumes that point mutations alter one nucleotide at a time, hence most of the instantaneous rates:
 - (3134/3761 or 84.2% in the case of the universal genetic code) are 0.
- This restriction, however, does not mean that the model disallows any substitutions that involve multiple nucleotides (e.g., ACT → AGG).
 - This can be further relaxed with models supporting multiple nucleotide changes.
- Such substitutions must simply be realized via several single nucleotide steps,
 e.g., ACT⇒AGT⇒AGG
- In fact the (i,j) element of $T(t) = \exp(Qt)$ sums the probabilities of all such possible pathways of duration t, including reversions
- Compare this to the naive NG86 parsimony approach.