The frequency of optimal codons (F_{op}) reflects the balance between the optimal to non-optimal codons synonymous substitution rate (K_{on}) and the non-optimal to optimal codons synonymous substitution rate (K_{no}):

$$\text{Non-optimal codon} \underset{K_{on}}{\overset{K_{no}}{\rightleftarrows}} \text{Optimal codon}$$

Substitution rates depend on the corresponding mutation rates (μ_{no}, μ_{on}) and fixation probabilities (P_{no}, P_{on}):

$K_{no}=2N_e\mu_{no}P_{no}$ *and* $K_{on}=2N_e\mu_{on}P_{on}$

where N_e is the effective population size.

Fixation probabilities are given by:

$P_{no}=\frac{1-e^{-4N_e f_0 s}}{1-e^{-4N_e s}}=\frac{1-e^{-2s}}{1-e^{-4N_e s}}\overset{s\to 0}{\approx}\frac{2s}{1-e^{-4N_e s}}$ similarly $P_{on}\overset{s\to 0}{\approx}\frac{-2s}{1-e^{4N_e s}}$

Where s is the selection coefficient in favor of optimal codons and f_0 the allele frequency of a new arrival mutation ($f_0 = 1/2N_e$).

At equilibrium, the frequency of optimal codons is given by:

$$Fop=\frac{K_{no}}{K_{no}+K_{on}}$$

which can be written as:

$$Fop=\frac{2N_e\mu_{no}P_{no}}{2N_e\mu_{no}P_{no}+2N_e\mu_{on}P_{on}}=\frac{\mu_{no}P_{no}}{\mu_{no}P_{no}+\mu_{on}P_{on}}=\frac{\frac{\mu_{no}}{\mu_{on}}\frac{2s}{1-e^{-4N_e s}}}{\frac{\mu_{no}}{\mu_{on}}\frac{2s}{1-e^{-4N_e s}}+\frac{-2s}{1-e^{4N_e s}}}$$

Let us note lambda, the ratio of mutation rates: $\lambda=\frac{\mu_{no}}{\mu_{on}}$

$$Fop=\frac{\lambda}{\lambda+\frac{-(1-e^{-4N_e s})}{1-e^{4N_e s}}}$$

$$\frac{1}{Fop}=1+\frac{1}{\lambda}\times\frac{-(1-e^{-4N_e s})}{1-e^{4N_e s}}$$

$$\frac{1}{Fop}-1=\frac{1}{\lambda}\times\frac{-(1-e^{-4N_e s})}{1-e^{4N_e s}}$$

$$\frac{1-Fop}{Fop}\times\lambda=\frac{-(1-e^{-4N_e s})}{1-e^{4N_e s}}$$

$$\frac{Fop}{1-Fop}\times\frac{1}{\lambda}=\frac{1-e^{4N_e s}}{-(1-e^{-4N_e s})} \quad (1)$$

With the following simplification:

$$\frac{1-e^{4N_e s}}{-(1-e^{-4N_e s})}=\frac{1-e^{4N_e s}}{-\left(1-\frac{1}{e^{4N_e s}}\right)}=\frac{e^{4N_e s}\times(1-e^{4N_e s})}{(1-e^{4N_e s})}=e^{4N_e s}$$

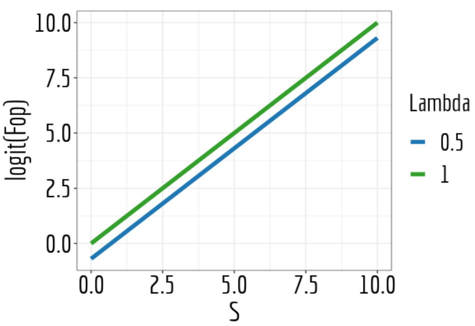
(1) → $\frac{Fop}{1-Fop}\times\frac{1}{\lambda}=e^{4N_e s}$

Thus, the population-scaled selection coefficient (S=4 $N_e s$) is given by:

$$S=\log\left(\frac{Fop}{1-Fop}\right)-\log(\lambda)=logit(Fop)-\log(\lambda)$$

Hence, we expect a linear correlation between *logit(Fop)* and *S*:

$$logit(Fop)=S+\log(\lambda)$$



If for weakly-expressed genes there is no selection, implied by the non-variation of *Fop* with gene expression, $S_{low\text{-}exp}$~0 :

$$logit(Fop_{low-\exp})=0+\log(\lambda)$$

$$logit(Fop_{high-\exp})=S_{high-\exp}+\log(\lambda)$$

$$S_{high-\exp}=logit(Fop_{high-\exp})-logit(Fop_{lox-\exp})$$