This notebook contains the proof that MutSel models will always correspond to a dN/dS≤1. The trick is to look at the forward and backward mutational path at the same time, i.e., we show that the total probability weight in going from i to j and going from j to i is always less than or equal to the sum of the frequencies of i and j.

Throughout this document, we write the frequency of amino acid i as x and the frequency of amino acid j as y. Further, we assume that x≤y. The fixation probability from x to y is:

In[81]:=
```
p[x_, y_] := (Log[y] - Log[x]) / (1 - x / y)
```

The sum of the probability weights going from x to y and from y to x is:

In[83]:=
```
Simplify[x p[x, y] + y p[y, x]]
```

Out[83]= $$\frac{2\,x\,y\,(\mathrm{Log}[x]-\mathrm{Log}[y])}{x-y}$$

We are going to show that this sum is less than or equal to x+y, i.e.,

$$\frac{2\,x\,y\,(\mathrm{Log}[x]-\mathrm{Log}[y])}{x-y}\leq x+y,$$

for x, y≥0 and x≤y.

To this end, we define the function

$$\mathrm{F}(x,\,y)\;=\;x+y-\frac{2\,x\,y\,(\mathrm{Log}[x]-\mathrm{Log}[y])}{x-y}$$

We thus want to show that F(x,y) ≥ 0 for x, y≥0 and x≤y. It is straightforward to show this for x=y:

In[92]:=
```
F[x_, y_] := x + y - (2 x y (Log[x] - Log[y]))/(x - y)
Limit[F[x, y], x → y]
```

Out[93]= 0

We now show that the first derivative of F(x, y) is negative throughout x ∈ (0, y), thus proving that F(x, y) has to be monotonically decreasing in this interval and hence has to be ≥ 0 in this interval.

In[108]:=
```
FullSimplify[∂x F[x, y]]
```

Out[108]= $$\frac{1}{(x-y)^2}\Big((x-3\,y)\,(x-y)+2\,y^2\,(\mathrm{Log}[x]-\mathrm{Log}[y])\Big)$$

We can rewrite Log[x]-Log[y] as a series:

In[101]:=
```
1/(x - y)^2 ((x - 3 y) (x - y) - 2 y^2 Sum[(1 - x / y)^n / n, {n, 1, ∞}])
```

Out[101]= $$\frac{(x-3\,y)\,(x-y)+2\,y^2\,\mathrm{Log}\left[\frac{x}{y}\right]}{(x-y)^2}$$

If we take only the first two terms of the series, we find that the expression becomes zero:

In[103]:=
```
Simplify[1/(x - y)^2 ((x - 3 y) (x - y) - 2 y^2 Sum[(1 - x / y)^n / n, {n, 1, 2}])]
```

Out[103]= 0

Thus, we can write the derivative of F(x, y) as:

$$\frac{-2\,y^2\,\mathrm{Sum}[(1-x/y)\hat{\ }n/n,\{n,3,\infty\}]}{(x-y)^2},$$

which is obviously negative.

Verification that the last statement was true:

In[106]:=
```
FullSimplify[1/(x - y)^2 -2 y^2 Sum[(1 - x / y)^n / n, {n, 3, ∞}]]
```

Out[106]=

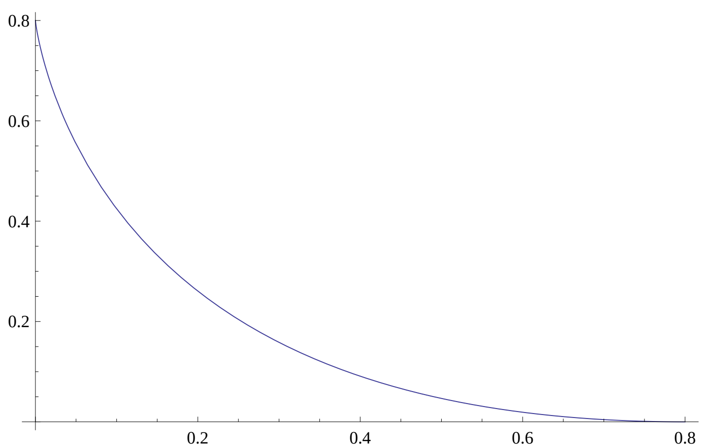
$$\frac{(x-3\,y)\,(x-y)+2\,y^2\,\mathrm{Log}\left[\frac{x}{y}\right]}{(x-y)^2}$$

This concludes the proof.

```
(*Plot showing that F[x, y] is positive.*)

Plot[x + y - (2 x y (Log[x] - Log[y]))/(x - y) /. y → .8, {x, 0, .8}]
```

Out[86]=



In[130]:=
```
(*Plot showing that the derivative of F[x, y] is negative,
and that the partial sums approximate it from above.*)
```

$$\text{Plot}\left[\left\{\frac{(x-3y)(x-y)+2y^2(\text{Log}[x]-\text{Log}[y])}{(x-y)^2} \text{ /. } y \to .5,\right.\right.$$
$$\frac{1}{(x-y)^2}(-2\,y\text{^}2\,(\text{Sum}[(1-x/y)\text{^}n/n, \{n, 3, 3\}])) \text{ /. } y \to .5,$$
$$\frac{1}{(x-y)^2}(-2\,y\text{^}2\,(\text{Sum}[(1-x/y)\text{^}n/n, \{n, 3, 5\}])) \text{ /. } y \to .5,$$
$$\left.\frac{1}{(x-y)^2}(-2\,y\text{^}2\,(\text{Sum}[(1-x/y)\text{^}n/n, \{n, 3, 7\}])) \text{ /. } y \to .5\right\},$$
$$\left.\{x, 0, 0.5\text{`}\}, \text{PlotStyle} \to \{\text{Black, Blue, Red, Green}\}, \text{PlotRange} \to \{-5, 0\}\right]$$

Out[130]=