Anaylsis of the Subfunctionalization Model for the Fate of Gene Duplicates

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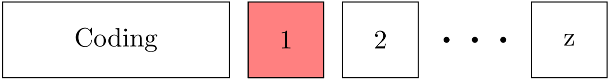

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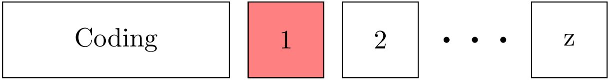

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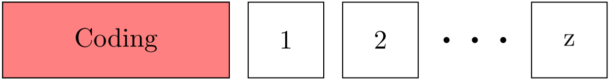

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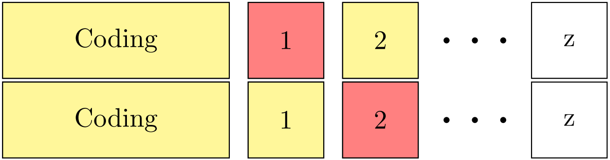

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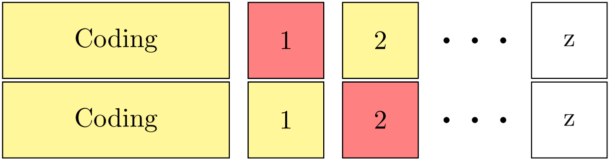

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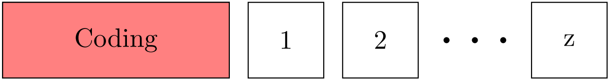

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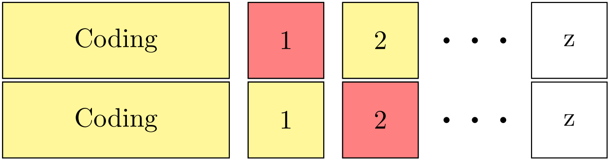

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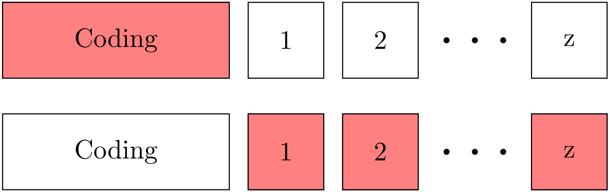

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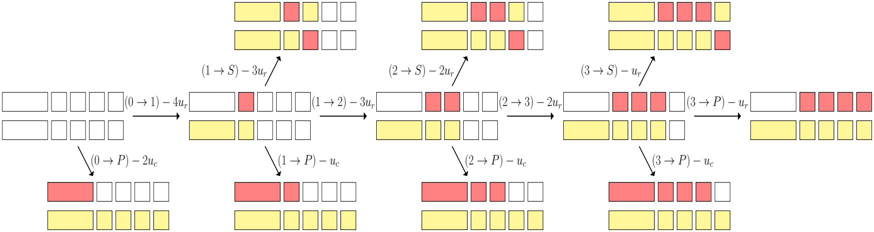

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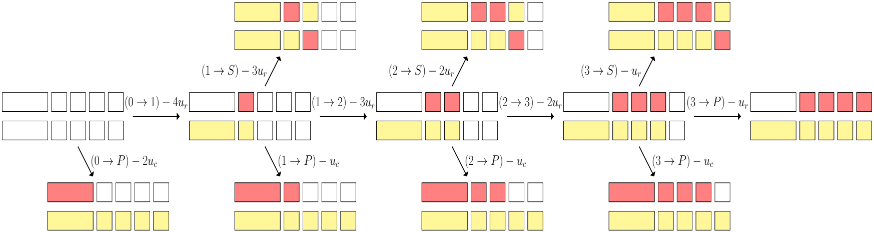

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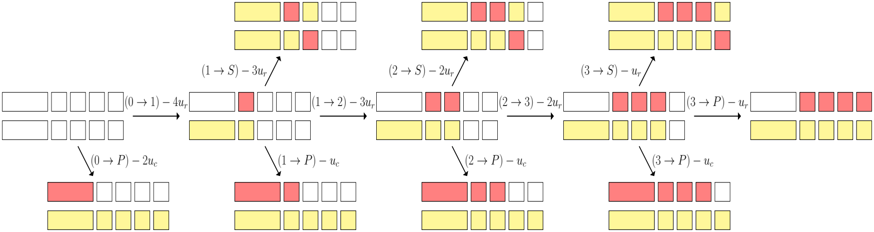

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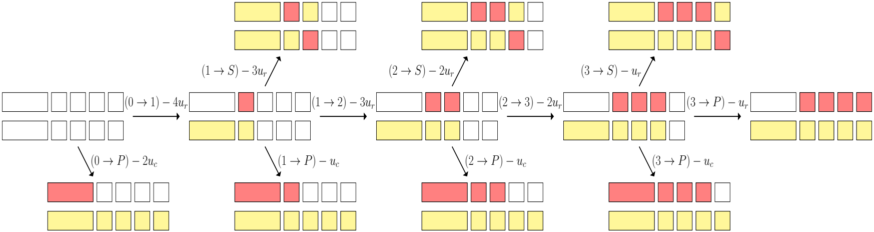

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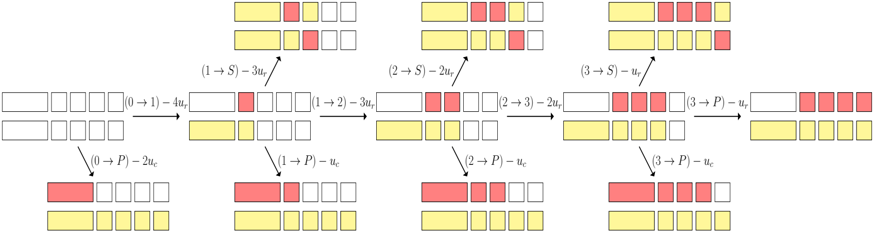

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- Rate of Subfunctionalization equals rate of transition to $i + 1$ equals $(z - i)u_r$.

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The structure of this CTMC is much like those that give rise to the phase-type distribution.

Generator as block matrix

For CTMCs of this structure, it is convenient to write

$$\mathbf{Q} = \left[\begin{array}{c|c} \mathbf{Q}^* & \mathbf{V} \\ \hline \mathbf{O} & \mathbf{O} \end{array}\right], \tag{2}$$

where $\mathbf{Q}^*$ contains the entries corresponding to transitions between transient states, and $\mathbf{V}$ transitions to absorbing states.

Some measures

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$$F_i(t) = 1 - \underline{\mathbf{e_i}} e^{\mathbf{Q}^* t} \underline{\mathbf{1}}. \tag{4}$$

With the density and cumulative distribution functions, we're able to derive results for various measures

- Probability of absorption into $j \in \{S, P\}$

$$\begin{aligned} p_{i,j} &= \int_{t=0}^{\infty} \underline{\mathbf{e_i}} e^{\mathbf{Q}^* t} \mathbf{V}_j dt \\ &= -\underline{\mathbf{e_i}} (\mathbf{Q}^*)^{(-1)} \mathbf{V}_j \end{aligned} \tag{5}$$

- The k^{th} moment of time until absorption

$$\begin{aligned} m_i^{(k)} &= \int_{t=0}^{\infty} t^k \underline{\mathbf{e_i}} e^{\mathbf{Q}^* t} \mathbf{V} \underline{\mathbf{1}} dt \\ &= (-1)^k k! \underline{\mathbf{e_i}} (\mathbf{Q}^*)^{(-k)} \underline{\mathbf{1}}, \end{aligned} \tag{6}$$

- Variance of time until absorption

$$var_i = m_i^{(2)} - (m_i)^2. \tag{7}$$

Cause-specific hazard rates

When there are several absorbing states, often interested in the cause-specific hazard rate

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Cause-specific hazard rate

$$\lambda_{ij}(t) = \lim_{h \to 0^+} \frac{P(t < T_{\{S,P\}} < t+h, X(T_{\{S,P\}}) = j | T_{\{S,P\}} > t, X(0) = i)}{h}$$
$$= \frac{f_{ij}(t)}{1 - F_i(t)} \quad = \frac{\underline{\mathbf{e_i}} e^{\mathbf{Q}^* t} \mathbf{V}_j}{\underline{\mathbf{e_0}} e^{\mathbf{Q}^* t} \underline{\mathbf{1}}} \tag{8}$$

$$\begin{aligned} f_i(t) &= \sum_{j \in \{S,P\}} f_{ij}(t), \\ \lambda_i(t) &= \sum_{j \in \{S,P\}} \lambda_{ij}(t). \end{aligned} \tag{9}$$

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So $\lim_{t\to\infty} \lambda_{ij}$ is surely $u_c + u_r$ for $j=P$ u_r for $j=S$.

We define the following:

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- The event that processes has not been absorbed by time t, but is absorbed by later time $t + h$
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Proof outline for $\lim_{t \to \infty} \lambda_{ij}$

First, note that

$$\lim_{t \to \infty} P(C_t | B_t, X(0) = i) = 1 \quad \text{and} \quad \lim_{t \to \infty} P(\overline{C}_t | B_t, X(0) = i) = 0,$$

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By Markov Property we can drop the t's, and we're left with $q_{z-1,j}$

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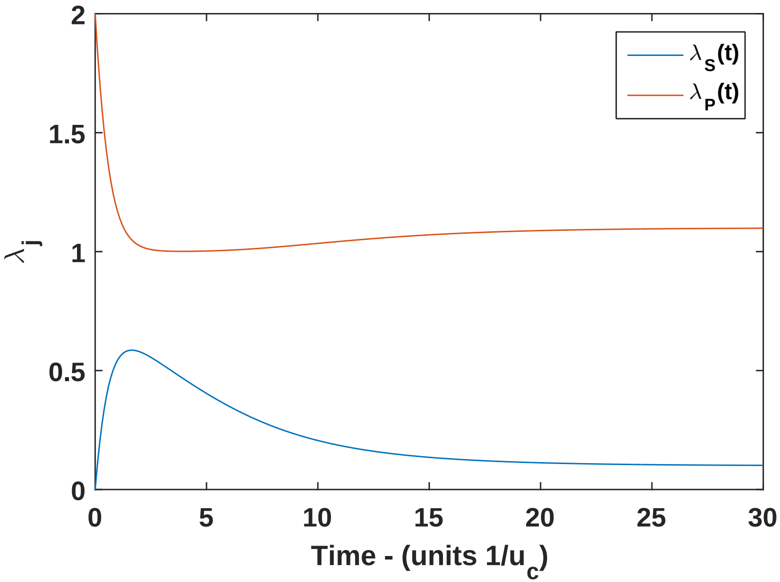

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Pseudogenization rate

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h_P^z(t) &= \lim_{h\to 0^+} \frac{P(t < T_P < t+h | T_P > t, X(0)=0)}{h} \\
&= \frac{f(t)}{1-F(t)} \\
&= \frac{\underline{\mathbf{e}}_0 e^{\mathbf{Q}^* t}\mathbf{V}_P}{1-\int_{u=0}^{t} \underline{\mathbf{e}}_0 e^{\mathbf{Q}^* u}\mathbf{V}_P du} \\
&= \frac{\underline{\mathbf{e}}_0 e^{\mathbf{Q}^* t}\underline{\mathbf{V}}_P}{1-\underline{\mathbf{e}}_0 \left(e^{\mathbf{Q}^* t}-\mathbf{I}\right)(\mathbf{Q}^*)^{(-1)}\mathbf{V}_P}.
\end{aligned} \tag{11}
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Here T_P is RV tracking time to absorption into P, and could be infinity.

Some limit analysis

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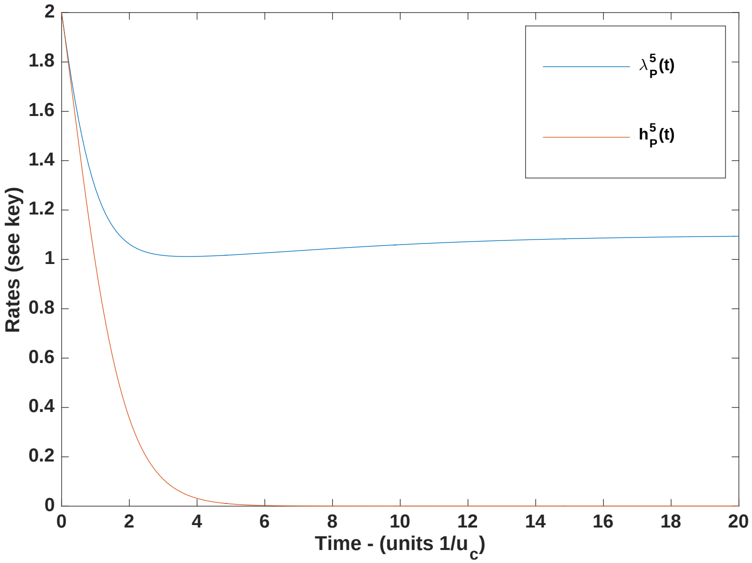
Wake up! A picture.



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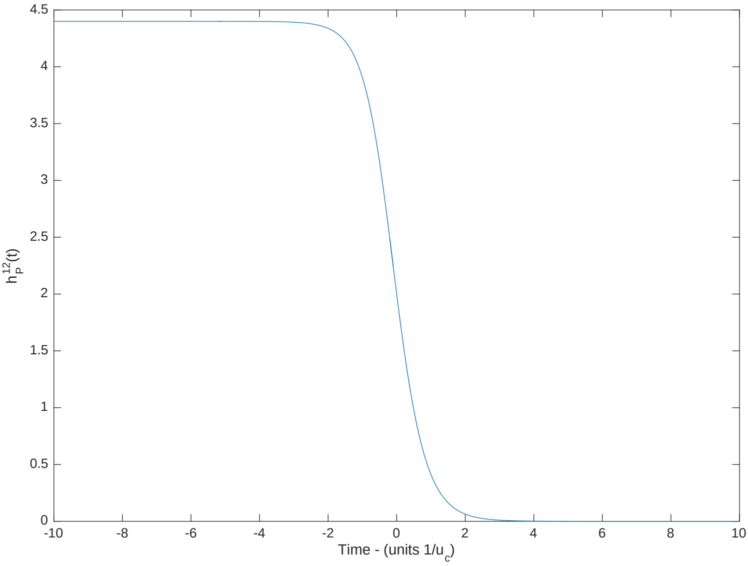
This motivates us to look into the behaviour of the model in negative time!

Sigmoid Function



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$h_P(t; \alpha)$ is an obvious generalization of our earlier function (rate of transition into absorbing state P assuming not already in P).

Using l'Hôpital's rule we get

$$\lim_{t \to -\infty} h_P(t; \underline{\alpha}) \quad = \quad \lim_{t \to -\infty} \frac{\underline{\alpha} e^{\mathbf{Q}^*} \mathbf{Q}^* \underline{\mathbf{V}}_P}{-\underline{\alpha} e^{\mathbf{Q}^* t} \mathbf{v}_P}. \tag{15}$$

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We diagonalize $\mathbf{Q}^*$

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Then we do some algebra to get

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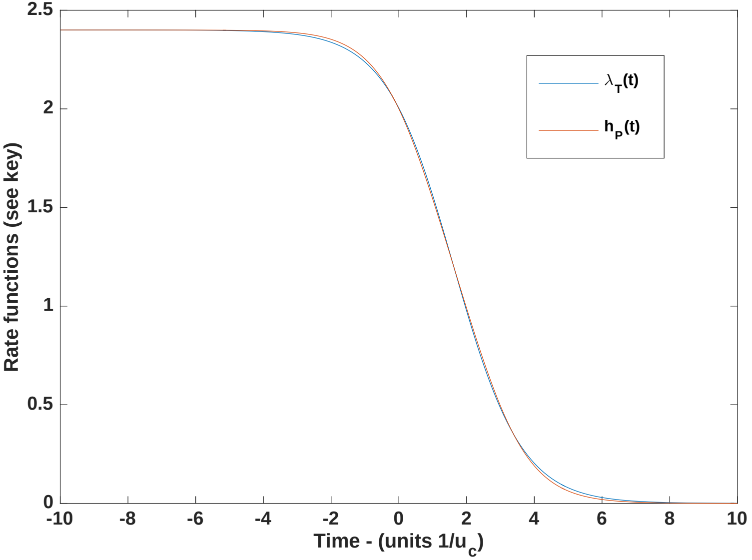
We can use this to fit the phenomenological approximation of Tuefel et al (2014) to our exact mechanistically function.

Phenom. vs Exact



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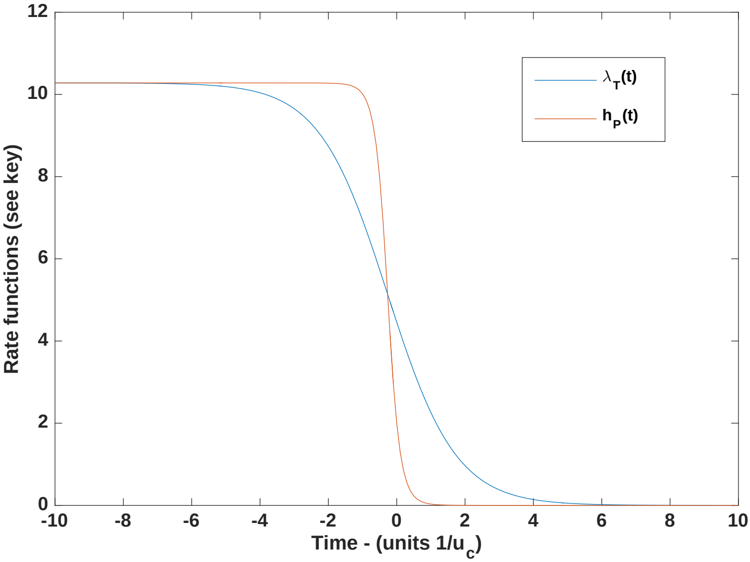

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- Expanding the model to allow for a mixture of sub- and neofunctionalization.