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Evolutionary Dynamics

Assignment #03

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1.1 Chromosomal instability

1.1.1 a

Calculate three ratios $C = \frac{CIN}{no-CIN}$ and show that C is independent of time 1. Neutral CIN : if we assume that genes with CIN are neutral (have no fitness advantages or disadvantages) we can conclude that mutation rate from state $A(+-) \to A(--)$ is Nu_2 and from $A(+-CIN) \to A(--CIN)$ is Nu_3. So we can create a linear ODE system. From lecture we know that its solutions for X_2 (i.e. A(–)) and Y_2 (i.e. A(– CIN)) are the following:

$$X_2(t) \approx Nu_1u_2 \times \frac{t^2}{2}$$

$$Y_2(t) \approx u_1u_ct^2$$

So, our rate is

2.1 Linear process of colonic crypt transformation

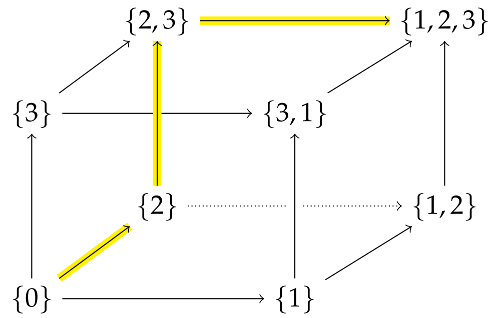
3.1 Multistage theory

4.1 Pathways of carcinogenesis

4.1.1 a

The probability of the path $P = 2 \to 3 \to 1$ for three independent mutations occurring after exponentially distributed waiting time $T_i \sim exp(\lambda_i), i = 1,2,3$ is:

$$P = J_1 \to \cdots \to J_k = J_2 \to J_3 \to J_1$$



$$\text{Prob(P)} = \prod_{i=1}^{3} \frac{\lambda_{Ji}}{\sum\limits_{J \in \text{Exit}_i} \lambda_J} = \frac{\lambda_2}{\sum\limits_{J \in \text{Exit}_i = 1,2,3} \lambda_J} \times \frac{\lambda_3}{\sum\limits_{J \in \text{Exit}_i = 1,3} \lambda_J} \times \frac{\lambda_1}{\sum\limits_{J \in \text{Exit}_i = 1} \lambda_J} = \boxed{\frac{\lambda_2 \lambda_3}{(\lambda_1 + \lambda_2 + \lambda_3) \times (\lambda_3 + \lambda_1)}}$$

4.1.2 b

All possible genotypes starting from the wt (no mutation occurred) are 8: $\{0\}; \{1,2,3\}; \{12,23,31\}; \{123\}$. Considering 2 out of 3 mutations one will obtain 6 possible pathways. Then, the expected waiting time is (where k is the number of mutations expected and p the number of pathways):

$$E[T_k] = \sum_{p=1}^{6} \sum_{n=1}^{k=2} \frac{1}{\sum\limits_{J \in \text{Exit}_i} \lambda_J} \times \text{Prob}(P) = \sum_{p=1}^{6} \sum_{n=1}^{k=2} \frac{1}{\sum\limits_{J \in \text{Exit}_i} \lambda_J} \times \prod_{i=1}^{3} \frac{\lambda_{Ji}}{\sum\limits_{J \in \text{Exit}_i} \lambda_J}$$

$$\begin{aligned} E[T_{p_{1-6}}] = {} & \left(\frac{1}{\lambda_1 + \lambda_2 + \lambda_3} + \frac{1}{\lambda_2 + \lambda_3}\right) \times \left(\frac{\lambda_1}{\lambda_1 + \lambda_2 + \lambda_3}\right) + \\ & + \left(\frac{1}{\lambda_1 + \lambda_2 + \lambda_3} + \frac{1}{\lambda_1 + \lambda_3}\right) \times \left(\frac{\lambda_2}{\lambda_1 + \lambda_2 + \lambda_3}\right) + \\ & + \left(\frac{1}{\lambda_1 + \lambda_2 + \lambda_3} + \frac{1}{\lambda_1 + \lambda_2}\right) \times \left(\frac{\lambda_3}{\lambda_1 + \lambda_2 + \lambda_3}\right) \end{aligned}$$

4.1.3 c

Considering d independent mutation, there are exactly $d \times (d-1) \times (d-2) \times \cdots \times 1 = d!$ pathways to the genotype where all the mutations are present at the same time. If cancer arises after k mutation, there are $d \times (d-1) \times (d-2) \times \cdots \times (d-k+1) = \frac{d!}{(d-k)!}$ paths.

5.1 Neutral Wright-Fisher process

6.1 Wave approximation