GENE DECAY

III. Mathematical Model of Back Mutations *

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Following previous application of mathematical models to the study of gene decay, as suggested by Gedda-Brenci's model of the ergon-chronon system, further results are reported, with special respect to a mathematical model of back mutations.

Every error produced by random agents in a DNA molecule may put in action a mechanism which is able to produce a back mutation of the molecule, i.e., to make the molecule efficient again (Watson 1965).

The study of gene decay with regard to back mutations is complicate: but the most difficult thing is to find the numerical data, for we don't know the probability that a mechanism be put in action. (The data we got about the velocity of the mutation process are comprehensive of the velocity of the back-mutation process.) Therefore, we can now only give qualitative consideration and get a formula which gives the probability $p(t)$ that a molecule be efficient at time t, with regard to both processes: either mutation and back mutation. Let us start with some considerations.

a) When a back-mutation mechanism is put in action by a random error (call γ the velocity of this process) it eliminates the entire nonefficient molecule and substitutes it with an efficient one, so that it cancels every error in the molecule. The mechanism acts instantaneously: we can disregard the time necessary for the substitution.

b) The mechanism can't correct the errors present in the molecule at the initial time $t = 0$.

Let us now calculate the probability $p(t)$ that a molecule be efficient at time t. Once we define the event A_t = a molecule is efficient at time t, we can write:

$$A_t = (B_t \cup C_t) \cap D \qquad [1]$$

where:

B_t = no errors in the molecule during time $(0, t)$;

C_t = an error in the molecule during time $(0, \tau)$, a back mutation at τ, no errors in (τ, t) ** $(0 \leq \tau \leq t)$;

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** We can neglect the possibility of more than one back mutation in a finite time t.

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D = a molecule is efficient at time $t = 0$.

We have a stochastic independence between the events D and $(B_t \cup C_t)$, and B_t and C_t are incompatible events; then we can write:

$$P(A_t) = P(D)\,[P(B_t) + P(C_t)] = p(t) \qquad [2]$$

$$p(t) = p\,[e^{-\bar{\mu}t} + \gamma \int_0^t (1 - e^{-\bar{\mu}t})\, e^{-\bar{\mu}(t-\tau)}\, d\tau] \ * \qquad [2']$$

$$p(t) = p\,\frac{\gamma}{\bar{\mu}} + p\, e^{-\bar{\mu}t}\,[1 - \gamma\,(p/\bar{\mu} + t)] \qquad [3]$$

We can now get the probability distribution of $M(t)$, i.e., the number of efficient molecules at time t.

The errors in different molecules are incorrelated, then we can write:

$$P(M(t) = h) = p_h(t) = \binom{20}{h} [p(t)]^h\,[1 - p(t)]^{20-h} \qquad [4]$$

We can also get the probability density function of the time of gene decay (see also Rossi 1972):

$$f(t) = \mu\,\frac{L+1}{20}\binom{20}{L+1}[p(t)]^{L+1}\,[1 - p(t)]^{20-(L+1)} \qquad [5]$$

and the expectation of time of gene decay:

$$E(t) = \mu\,\frac{L+1}{20}\binom{20}{L+1}\int_0^{+\infty} t\,[p(t)]^{L+1}\,[1 - p(t)]^{20-(L+1)}\, dt \qquad [6]$$

and the variance:

$$\sigma^2(t) = \mu\,\frac{L+1}{20}\binom{20}{L+1}\int_0^{+\infty} t^2\,[p(t)]^{L+1}\,[1 - p(t)]^{20-(L+1)}\, dt - E^2(t) \qquad [7]$$

If we consider:

$$\lim_{t \to +\infty} p(t) = p\,\frac{\gamma}{\bar{\mu}}$$

* $\bar{\mu} = \mu/20$ is the velocity of the mutation process in a molecule.

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we can get the asymptotic probability distribution of $M(t)$:

$$P(M(\infty) = h) = p_h(\infty) = \binom{20}{h} \left(p \frac{\gamma}{\bar{\mu}}\right)^h \left(1 - p \frac{\gamma}{\bar{\mu}}\right)^{20-h}$$

Such a distribution has its mode practically at $h = 0$ because of condition c).

Genetically speaking, we can neglect the asymptotic probability distribution of $M(t)$. In fact, gene decay is a stochastic process with an absorbent barrier at L; and it tends against such a barrier, so that it terminates, with probability 1, in a finite time.

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