derstanding the distribution (as opposed to the mean) of the replication timing for a given $I(t)$ and spatial distribution of potential origins. That is, knowing the average time it takes for replication to complete does not help; what one cares about is how often replication fails by taking longer than some threshold time $T$.

With this in mind, Bechhoefer and co-workers interpreted the time it takes to complete replication as a "first-passage" time $t$ of a stochastic process governed by probability $I(t)$, which concerns the distribution $r(t)$ of a probabilistic event of interest to occur for the first time at time $t$ or, equivalently, as the largest value $t$ of the timing of collisions between two growing replication bubbles. For biological success, $t$ does not have to be less than $T$ for every cell, but the frequency of $t > T$ has to be less that some acceptable failure rate. This question belongs to the domain of extreme-value statistics (a branch of statistics that is also used to evaluate things like rare but catastrophic events), and the random-completion problem can be translated into finding conditions where $I(t,x)$ results in the observed average time to complete replication and the observed failure rate [10].

Yang and Bechhoefer have provided the final, clear answer to the random-completion problem: For cells to achieve an acceptable distribution of replication completion times, the initiation rate $I(t)$ should increase during replication (Fig. 1), in agreement with extracted values of $I(t)$ from experimental data [8]. They show that this model can produce arbitrarily low failure rates, but more importantly, that it can produce the observed failure rate using plausible parameters that also produce reasonable mean completion times. And finally, Yang and Bechhoefer show that their result is robust; the increasing $I(t)$ produces timely replication regardless of whether the potential origins are randomly or nonrandomly distributed. This latter point should allay biologists' fear that in this model the replication time would double if one or two origins fail to initiate and create a gap that is too large to finish replication within 20 minutes.

Given the strong theoretic foundation provided by Yang and Bechhoefer for the increasing $I(t)$ model in frog embryos, the big question is whether this model is applicable to all animal cells. Much of this work will fall to the experimental biologists, but theoretical treatments that capture the more structured replication of adult cells will certainly be important.

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## About the Authors

### Suckjoon Jun