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Stochastic model for error propagation over multiple cell generations

Chromosome segregation during cell division is carefully choreographed to ensure equal partitioning of the duplicated genetic material. If this process fails to occur accurately, the resulting daughters might have karyotype imbalance, known as aneuploidy. Even though mitotic errors have been studied extensively, the mechanisms generating various errors, their propagation and effects on genome integrity are not well understood. Here we develop a stochastic model that describes error propagation through many cell generations and its effect on cell vitality. For each cell division, the model considers the state of the mother cell, to predict the state of the daughter cells. The state of a cell is determined by the number of chromosomes and following mitotic surveillance mechanisms: attachment error-correction (EC), spindle assembly checkpoint (SAC) and apoptosis. Using this model, we describe the evolution of a cell's state over the generations. This allows us to give predictions about the contribution of surveillance mechanisms in a cell which will lead to a lower error rate to maintain cell viability. Model predictions will be tested experimentally which will help us understand how mitotic errors arise, how they propagate and how they impact on cell populations. Taken together, the model will provide a consistent explanation for aneuploidy in healthy and cancer cells and tissues.

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