



Multicellular survival as a consequence of Parrondo's paradox

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In the face of inevitable aging and death, Nelson and Masel (NM) (1) argue that alternating life history stages between multicellularity and unicellularity enable the survival of multicellular lineages. This is exactly parallel to the game-theoretic Parrondo's paradox (2), in which two individually losing strategies are temporally intercalated to yield winning outcomes. Originally conceived as an abstraction of flashing Brownian ratchets (3), the paradoxical theoretical framework has been greatly extended into ecology and evolutionary biology. For instance, the alternation of ecological populations between nomadic and colonial behaviors has been shown to be critical in allowing survival amidst resource scarcity (4).

In the present context, both a relaxation and intensification of intercellular selection pressure are losing strategies. The former admits the accumulation of senescent cells; the latter promotes cheater proliferation. Temporally alternating between unicellularity during reproduction, which entails heavy intercellular competition, and multicellularity with reduced selection pressure yields an overall winning strategy. Such a process may also be framed as a Parrondo-like ratcheting mechanism. Cellular vigor and cooperative traits are ratcheted forward during the unicellular and multicellular phases, respectively, but undergo diffusion during the succeeding complementary phase; these are individually analogous to the particle dynamics in flashing Brownian ratchets.

Crucially, the aging and death of an organism are necessary for the survival of its lineage. NM (1) indicate that life persists in spite of inevitable aging; we instead argue that life persists because of aging and death. The

possibility that aging is imperative for the survival of a species, and hence a universal target for selection, was neglected by NM. It is not that evolution is bypassed, as claimed by Mitteldorf and Fahy (5), but that the entire life cycle is subject to optimization through natural selection (6), including aging and death.

Parrondo's paradox in aging completes a much larger picture emergent from its application in adjacent biological fields (4, 7, 8). We believe we are close to uncovering a universal law in biology, but such is not a "negative universal" as suggested by Wagner (9), because it confers ultrastructural unity for the vast diversity of biological systems. It positively predicts that the losing games of solitary cells, organisms, and species add up to a winning virtual immortality for life itself: The units of life experience necessary and inevitable senescence, but the biosphere does not. Cells come and go, but the body persists; bodies come and go, but the species persists; species come and go, but the biosphere persists.

Positive universality implies rich empirical applicability across vastly different temporal and spatial scales. At every examined scale, cyclic subsidence and growth selects traits that are otherwise mutually exclusive, thereby supporting the persistence of the next-largest scale. In tandem with selectable variation, this recurrent, fractal-like hierarchy of Parrondo effects supplies robustness to the biosphere, enabling the outflanking of extinction for billions of years. In this respect, the letters (5, 10) are not contradictory to NM (1); they are differing, true, but incomplete vantage points on a system of staggering scale, complexity, and beauty.

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