

21 Grams

A Theoretical Proposal for Studying the Energy Balance of the Transition from Life to Death

Abstract

This paper proposes studying the transition from life to death through the energy balance of a single cell. The comparison spans an interval between a state identified as living and a state identified as dead, without assuming that the precise moment of transition can be determined. The aim is to establish whether exchanges with the environment and changes in the energy contained within the system can be fully accounted for through independent measurements. An energy balance that closed within measurement uncertainty would be consistent with an understanding of life as the dynamic organisation of matter, without establishing that this is the only possible interpretation. The paper outlines a theoretical design, clarifies its limitations, and identifies the conditions required for a future investigation.

Keywords: life; death; energy balance; biological organisation; thermodynamics.

1. The Question

What happens when an organism dies?

If we compare the same organism at two closely spaced moments, before and after the irreversible loss of its vital functions, we do not necessarily observe an appreciable change in mass or an abrupt alteration in its material composition. Chemical transformations and energy exchanges continue briefly after death. What is lost is the organism's capacity to sustain and coordinate the processes through which it maintained its own existence.

Death is not necessarily an instantaneous, uniform event: in complex systems, the cessation of the organism's functions may precede that of its individual cells. Even in a unicellular organism, such as a ciliate, observing changes in movement and structure is not, on its own, sufficient to determine the exact moment of death¹.

In 1907, Duncan MacDougall sought to determine whether death was accompanied by the loss of a substance possessing mass by weighing six dying patients. The alleged finding of "twenty-one grams", to which the title alludes, serves here only as a rhetorical point of departure. Despite its enduring presence in popular culture, the study provided no scientifically reliable evidence, owing to limitations in the sample, the measurements, and the identification of the moment of death².

The question can nevertheless be approached from another perspective, without presupposing the existence of a "substance" that leaves the body. At death, the organism's material constituents do not disappear; they continue to undergo physical and chemical transformations. What is lost is the capacity to sustain and coordinate the processes that maintained the living system.

¹ This video shows the progressive disintegration of a unicellular organism: <https://youtu.be/ibpdNqrtar0> (all links last accessed on 6 October 2026).

² D. MacDougall, Hypothesis concerning soul substance together with experimental evidence of the existence of such substance, *Journal of the American Society for Psychical Research*, 1(5), 1907.

2. A Thermodynamic View of Life

There is no universally accepted definition of life. Likewise, defining death presents difficulties, particularly in borderline cases. In many situations, we can distinguish a living system from a dead one with considerable confidence, while identifying the precise moment at which life emerges or vital functions cease may be more difficult. Death can be described as a process whose boundaries depend on the criteria adopted. Can a thermodynamic perspective help us understand what changes during this transition?

An organism exchanges matter and energy with its environment. It uses these exchanges to maintain its structure, repair itself, and perform its vital functions. Its organisation therefore requires continuous activity.

In *What Is Life?* (1944), Schrödinger describes a living organism as a system that maintains its organisation through exchanges with the environment. An organism can preserve local order without violating the second law of thermodynamics, provided that the overall balance for the organism and its environment remains consistent with that law³. Prigogine's theory of dissipative structures provides a framework for understanding how, under certain conditions, flows of energy and matter can sustain ordered configurations far from equilibrium. When the conditions that sustain them cease to hold, these configurations can dissolve without the loss of an additional material constituent⁴. Nair-Collins interprets death as the loss of the organism's capacity to maintain homeostasis and counteract processes of degradation.

On this account, death does not coincide with the immediate attainment of thermodynamic equilibrium: it marks the loss of the capacity to resist that equilibrium as an organised system⁵. Many reactions continue, and relaxation towards equilibrium may take a long time.

The proposal advanced in this paper therefore builds on a body of research that already examines the energetic aspects of life and cellular death⁶. These studies provide relevant methods and precedents. However, the specific experimental question proposed here does not appear to have been formulated in the works examined: whether a complete energy balance can be reconstructed between a state identified as living and a state identified as dead in the same cell, in order to investigate the possible presence of unaccounted energy contributions.

3. What to Measure

The first law of thermodynamics does not state that an organism's energy remains constant. It states that changes in its energy must correspond to exchanges with the environment. The question is therefore not whether the body has the same energy before and after death, but whether the observed changes are fully explained by the exchanges and transformations accounted for.

³ E. Schrödinger, *What Is Life? The Physical Aspect of the Living Cell*, Cambridge University Press, 1944.

⁴ I. Prigogine, I. Stengers, *La nouvelle alliance. Métamorphose de la science*, Gallimard, 1979.

⁵ M. Nair-Collins, *We Die When Entropy Overwhelms Homeostasis*, in M. Cholbi and T. Timmerman (eds.), *Exploring the Philosophy of Death and Dying: Classical and Contemporary Perspectives*, Routledge, 2021.

⁶ Hunt and colleagues (K. A. Hunt, F. von Netzer, D. Gorman-Lewis, D. A. Stahl, *Microbial maintenance energy quantified and modeled with microcalorimetry*, *Biotechnology and Bioengineering*, 119(9), 2022. <https://doi.org/10.1002/bit.28155>) use microcalorimetry to quantify microbial maintenance energy; Schiraldi (A. Schiraldi, *Short- and Long-Term Evolution of Microbial Cultures: A Thermodynamic Perspective*, *International Journal of Molecular Sciences*, 26(9), 2025. <https://doi.org/10.3390/ijms26094187>) also considers culture decay from a theoretical perspective, while Himeoka and colleagues (Y. Himeoka, S. A. Horiguchi, T. J. Kobayashi, *Theoretical basis for cell deaths*, *Physical Review Research*, 6, 2024. <https://doi.org/10.1103/PhysRevResearch.6.043217>) propose a theoretical formalisation of cellular death as a problem of controllability: a state is dead if the cell can no longer be returned from it to a living state.

The balance can be expressed simply:

$$\text{Initial energy} + \text{energy entering} = \text{final energy} + \text{energy leaving}$$

Initial energy is the energy contained within the system at the selected moment when the cell is identified as living; final energy is the energy contained within the same system at the selected moment when it is identified as dead. Energy entering and leaving includes all exchanges with the environment over the interval. If the two sides agree within measurement uncertainty, the balance closes. Its terms must be determined independently: agreement cannot be obtained by imposing it in the calculation.

The system's boundaries must be precisely defined. The system might comprise the cell and its surrounding medium within a small vessel. If the vessel is closed to exchanges of matter, the nutrients already present contribute to the initial energy, and the products remaining within it contribute to the final energy. Heat and any other transfers across the vessel's boundaries must instead be counted as exchanges with the environment. Calorimetry alone is insufficient to reconstruct the entire balance. A cell contains chemical energy and electrical and ionic gradients; measuring the heat it produces does not reveal every change in its energetic state. Cellular bioenergetics studies energy fluxes, their distribution, and the constraints they impose on biological processes⁷.

4. A Possible Experimental Design

The ideal system for this investigation is a single cell, such as a ciliate, observed without an intervention intended to cause its death⁸. This choice makes it possible to follow the same organism throughout the transition and avoids overlapping death events across multiple cells. A culture would make an aggregate signal easier to detect, but would also make it more difficult to attribute that signal to the transition of an individual organism from life to death. For this theoretical design, the conceptual advantage of studying a single cell takes precedence, although the instrumental difficulties remain unresolved.

Observation would begin at a time t_1 when the cell is identified as living and continue until a time t_2 when it is identified as dead, according to explicit and agreed biological criteria for the organism selected. There would be no need to know in advance where death occurs within this interval: the investigation would follow what happens between the two endpoints.

The balance would encompass all exchanges and transformations between t_1 and t_2 . It would not presuppose an abrupt change at a precisely defined instant. Residual metabolism and cellular degradation would contribute to the signal: even after death, chemical reactions may continue to generate heat. Selecting these two endpoints avoids the need to locate the transition exactly, but does not, by itself, allow any discrepancy observed during the interval to be attributed to death.

The investigation would have two aims: to test whether the energy balance closes between the two states, and to describe how energetic activity evolves during the transition. Appropriate controls, calibrations, and an estimate of overall uncertainty would be required, alongside validation of the biological criteria used.

⁷ X. Yang et al., Physical bioenergetics: Energy fluxes, budgets, and constraints in cells, *Proceedings of the National Academy of Sciences*, 118(26), 2021, e2026786118. <https://doi.org/10.1073/pnas.2026786118>.

⁸ Zhu and colleagues (H. Zhu et al., A low-cost picowatt calorimeter using a flexible printed circuit board, *Nature Communications*, 16, 2025. <https://doi.org/10.1038/s41467-025-58025-9>) record the heat produced by ciliates during a dehydration process that leads to death. Their work demonstrates that calorimetry involving only a few ciliates is already feasible. In contrast to the design proposed here, death is induced by dehydration, and the measurement concerns heat flow rather than the closure of an energy balance.

Measuring energy exchanges and changes in a single cell with sufficient precision remains a central difficulty, to be addressed in any subsequent development of the design by specialists.

5. Possible Results and Limitations

If the balance closed between the living and dead states, no unaccounted energy contribution exceeding the detection limits would be found. The result would provide empirical support for the possibility of describing the transition in terms of transformations of matter and the loss of the organisation that sustained vital functions. It would not establish that this description exhausts the nature of life, but would place a quantitative limit on the hypothesis of an additional energetic component that is lost at death.

If a systematic and reproducible discrepancy emerged, the completeness of the model and the reliability of the measurements would need to be examined first. An anomaly that persisted after these checks would indicate that the adopted energetic description was incomplete. Establishing whether it specifically concerned death would require further comparisons capable of distinguishing it from other processes occurring during the interval.

The value of the proposal therefore lies in making at least part of the question of the nature of life amenable to empirical investigation. A complete balance could establish the limits within which the transition can be explained by the physical processes accounted for; a confirmed discrepancy would indicate where further investigation is needed. In either case, the contribution would be to clarify what changes at death and which hypotheses about that change can be put to the test.

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