On a theory of cell decision-making for multicellular systems

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Cell decision-making is the process of cells changing their phenotype according to their intrinsic programming and in response to the microenvironmental cues. Currently, little is known about the principles dictating cell decision-making in multicellular systems. Regarding cells as Bayesian decision-makers under energetic constraints, we propose that organisms of all domains of life operate using a 'Least microEnvironmental Uncertainty Principle' (LEUP) for their decision-making processes. This is translated into a free-energy principle, implying a statistical mechanics theory for cell decision-making. Here, we address three fundamental challenges: (C1) the uncertainty/stochasticity of subcellular regulatory cell decision-making mechanisms, (C2) lack of knowledge in the relative contribution of intrinsic and extrinsic cell decision-making factors to multicellular spatiotemporal dynamics, and (C3) a unified theory for different types of cell decision-making. Such a statistical mechanics reduction allows for simplifying many parameters into a low-dimensional mathematical description and circumvent the uncertainty about the underlying mechanisms. .