On a theory of cell decision-making in multicellular systems: the least microenvironmental uncertainty principle

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Cell decision-making is the cellular process of responding to microenvironmental cues. This can be regarded as the regulation of cell's intrinsic states to extrinsic stimuli. Currently, little is known about the principles dictating cell decision-making in the context of multi- cellular systems. Regarding cells as Bayesian decision-makers under energetic constraints, I postulate the principle of least microenvironmental uncertainty (LEUP). This is translated into a free-energy principle and I develop a theory cell decision making in multicellular systems. Initially, I show that LEUP is compatible with the intrinsic state entropy minimization for differentiating cells. Finally, I will provide examples of LEUP in the context of tissue development and cancer growth.