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Construction of A Self-consistent Landscape for Multistable Gene Regulatory Circuits MINGYANG LU, JOSE ONUCHIC, Rice University, ESHEL BEN-JACOB, Tel-Aviv University — Cell fate decisions during embryonic development and tumorigenesis pose a major research challenge in modern developmental and cancer biology. Cell fate decisions between different phenotypes are regulated by multistable gene circuits that give rise to the coexistence of several stable states. Internal and external noise play crucial role in determining the transitions between and the relative stability of the coexisting phenotypes. The deterministic dynamics of these circuits is not derivable from a potential. Yet, motivated by Waddington Epigenetic Landscape, many rely on the notion of effective potential to describe cell fate determination in the presence of noise. Here, we present a construction of a self-consistent landscape (effective potential, W $\equiv$ -ln(probability)), utilizing the Eikonal equation approach (WKB approximation of the corresponding Fokker Planck equation) for the cases of white noise and shot noise. The approach is based on utilizing the method of characteristics in a special way. We also devised a numerical method to efficiently calculate the contour of the potential and the optimal path for the transitions from one stable state to another. We tested the method on the bistable and tristable double inhibition circuits, and we showed that the constructed landscape agrees very well with the numerical simulation of the stochastic equations. We expect this method to be valuable to a wide range of multistable gene circuits.

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