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Predicting TGF-β-induced epithelial-mesenchymal transition using data assimilation

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Presenter Information

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Epithelial-mesenchymal transition (EMT) is a fundamental biological process that plays a central role in embryonic development, tissue regeneration, and cancer metastasis. The main characteristic of EMT is the transdifferentiation of an epithelial cell to a mesenchymal cell, which includes losing epithelial-type cell-cell adhesion and gaining the mesenchymal-type enhanced cell motility. Transforming growth factor-β (TGF-β) is a major and potent inducer of this cellular transition, which is comprised of two state transitions, first from an epithelial state to an intermediate or partial EMT state, then from the partial state to a mesenchymal state. Experimentally, it is typically not possible to observe more than two EMT cell markers at the same time, which makes predicting the timing of state transitions inherently difficult. Here, we propose a data-assimilation approach, which combines limited noisy observations with predictions from a computational model of TGF-β-induced EMT, to reconstruct the full experimental system and predict the timing of the partial-to-mesenchymal state transition. We tested our approach in proof-of-concept "synthetic" *in silico* experiments, in which experimental observations were produced from a computational model with the addition of noise. We varied several properties of the data-assimilation approach including the numbers of ensemble members on our forecast system and the time interval between observations. We found that under ideal conditions, the partial-to-mesenchymal transition time could be predicted after 1 day of observations, approximately 11 days before the transition. Additionally, we found that decreasing the time interval between observations typically reduced prediction error. Future work will include testing and optimizing our approach over a wider range of physiological conditions and ultimately testing against *in vivo* experimental data.