

Boolean modelling of protein translocations reveals compartment-specific perturbations altering the fate of epithelial-mesenchymal transition

Márk Kerestély¹, Péter Mendik¹, Sebestyén Kamp², Dávid Deritei¹, Nina Kunšič¹, Péter Csermely¹, Daniel V. Veres^{1,2}

¹ Department of Molecular Biology, Institute of Biochemistry and Molecular Biology, Semmelweis University, Budapest, Hungary

² Turbine Ltd. Budapest, Hungary

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Protein translocations between subcellular compartments (e.g., nucleus, cytoplasm) have a crucial role in the orchestration of complex signalling processes like the epithelial-mesenchymal transition (EMT), which is significant in cancer progression. We defined a compartmentalized approach to simulating Boolean signalling networks to explore the compartment-specific functions of translocating proteins in EMT. These functions could serve as novel drug targets, and compartmentalized networks are needed for their investigation.

As a proof-of-concept depicted in *Figure 1*, we compartmentalized a previously established Boolean EMT model by conducting a literature review and manual curation of translocating EMT proteins aided by the predictions of our Translocatome database. We outlined a complex readout of the dynamic simulations of the model, which included the visualization of node activities, signalling pathway activities and attractor states.

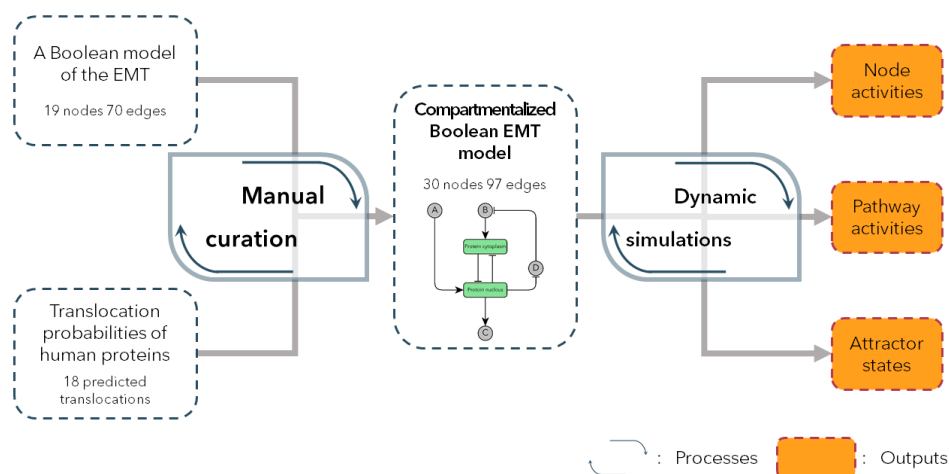


Figure 1: Workflow utilized in the compartmentalization of a Boolean EMT model

Results from our dynamic simulations predicted that when localized in the nucleus, glycogen synthase kinase-3 beta (GSK3B) translocating protein has a greater inhibitory effect on the transforming growth factor beta-1 (TGFB) mediated EMT. Our model also reinforced that the nuclear activation of glioma associated oncogene transcription factors (GLI) is required for a complete EMT. These results demonstrate the importance of differentiating the functions of translocating proteins by their subcellular localization in network models.