

Local sensitivity analysis of GLUT4 translocation in response to insulin

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When developing a mathematical model of a biological system there is an inherent tension between the desire to fully represent the underlying complexity of the biological system and the need to reduce the model to achieve computational tractability. On the one hand, we wish the model to provide insight into the physiology of the system, and hence the inclusion of a certain degree of biological complexity is vital. However, the inclusion of excessive biological detail can itself obscure the clarity we are aiming to achieve.

Here we present a middle path between these two extremes. We establish a simple method of local sensitivity analysis to investigate the behaviour of an extant phenomenological model of GLUT4 translocation in response to insulin. We have developed metrics that provide mathematically and physiologically meaningful measures of the model output. These metrics were used to identify critical nodes in the network and provide insight into the regulation of the system. Just as importantly, however, insensitive nodes were identified, leading to the development of a reduced parameter set. In the future, this reduced parameter set will form the basis of a global sensitivity analysis of the system, and potentially contribute to structural improvements in the model in the light of new understanding of the interactions in the system.