

SiViT

Signalling Visualisation Toolkit

The Signalling Visualisation Toolkit (SiViT) is a cancer cell signalling network visualisation tool that provides an intuitive, games-based, real-time interactive interface to models of cancer cell dynamics. SiViT provides a games technology approach to unlocking the complexities of cancer cell responses to anti-cancer drugs. While SiViT is able to load a wide range of biological models in the form of SBML, our research focuses on a particular network commonly linked to cancer. SiViT allows clinicians and biologists to directly interact with the cancer cell model, introducing drugs and cancer-causing mutations through a menu interface. SiViT animates the effects of these drugs and mutations on the cell signalling pathways and nodes. The animations show how the cell network responds to these drugs and mutations, and responses include increases and decreases in activity, oscillations and re-rerouting to bypass the effected region of the network. The network animations indicate the effectiveness of drugs and the emergence of drug resistance, suggesting opportunities for further experimental studies.

SiViT offers bi-directional interaction and explorations, updating the underlying computational model and corresponding visualisation in real time. Consideration of the timings and combinations of drug additions or mutations are crucial in anti-cancer drug design, and SiViT allows for multiple changes to occur at specific timings, modelling and then visualizing the result. This real-time exploration can contribute to the identification of combination therapies, a route to overcome anti-cancer drug resistance. SiViT adheres to visual guidelines from existing literature on cell networks and dynamics.

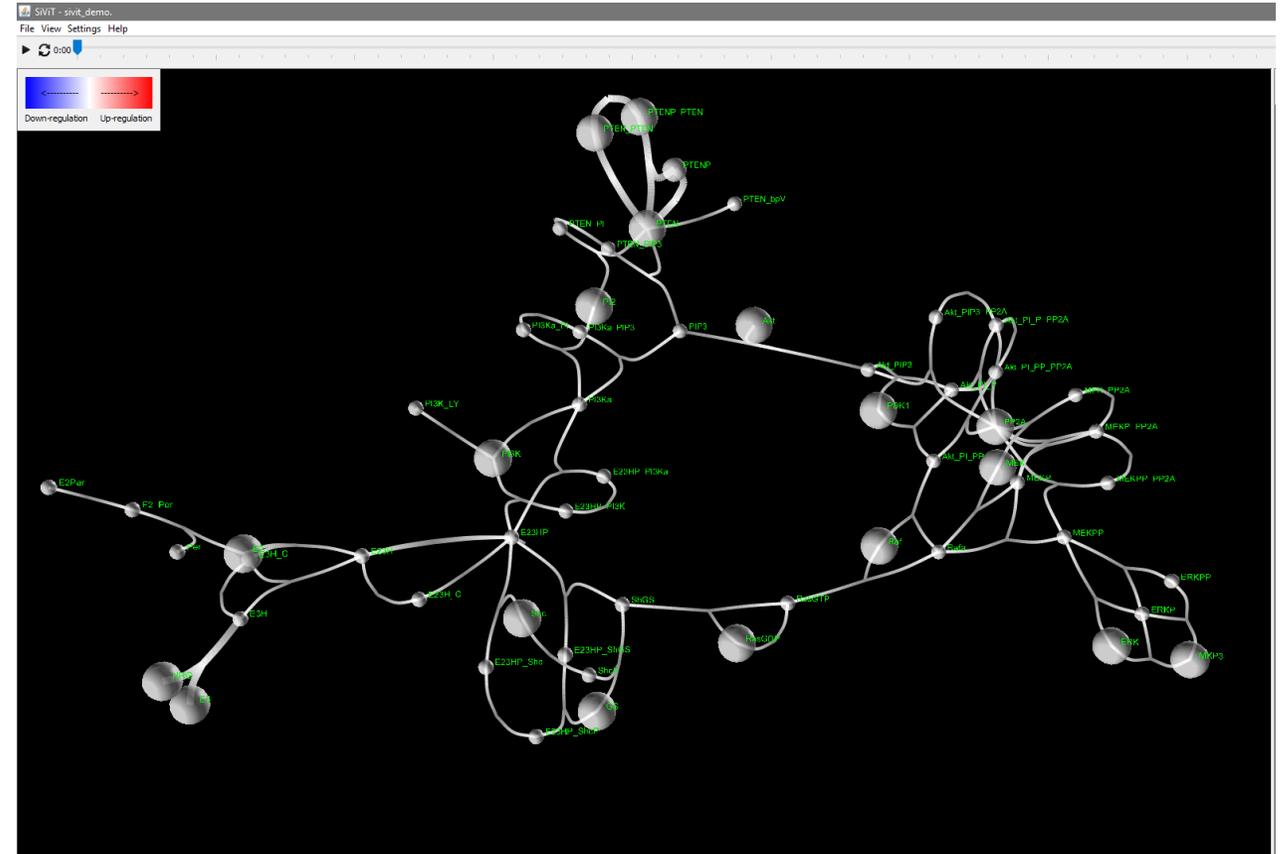
SiViT was part of the UKRI Main Exhibition Stand at the American Association for the Advancement of Science 2019 conference. SiViT was the catalyst for a new 4-year project led by Macmillan Cancer Support on optimising health and social care service provision through interactive network visualisation.

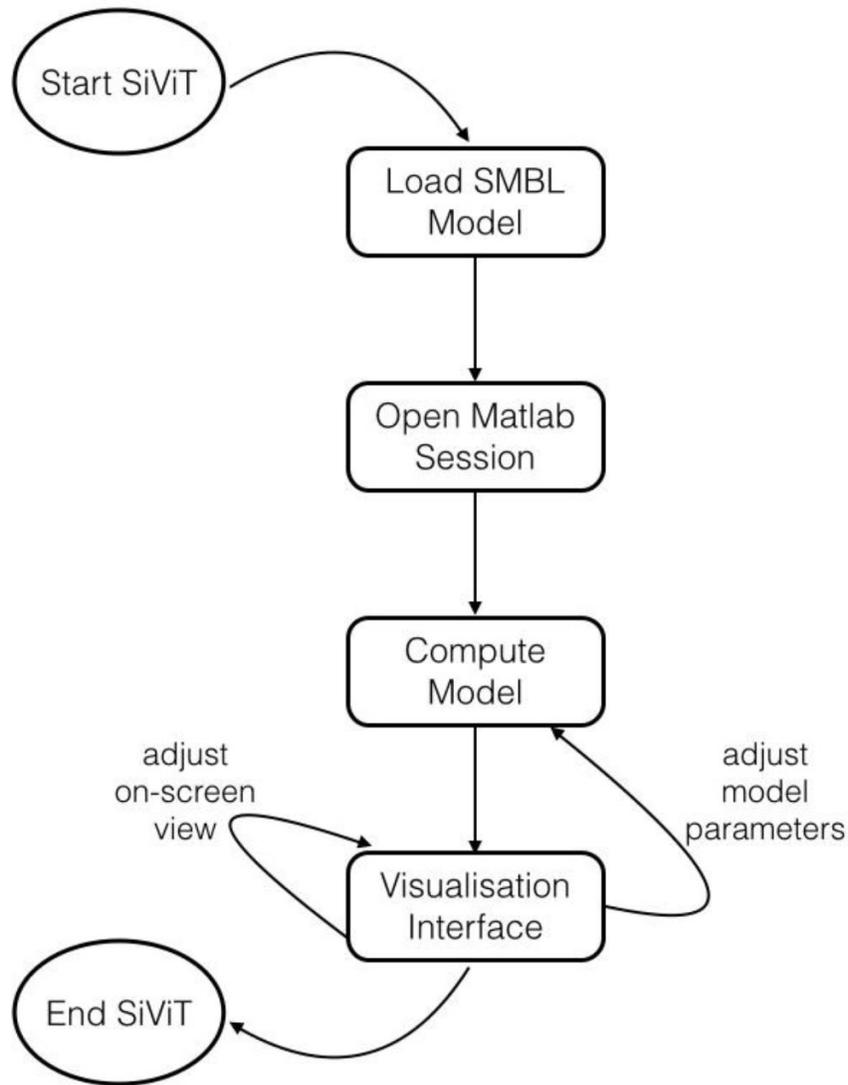
SiViT Model

Drawing on computer games technology for real-time and interactive visualisation of data, SiViT converts systems biology models of cancer cell signalling into interactive simulations that can be used without specialist computational expertise.

SiViT is generalizable and accessible, supporting preclinical research, combinatorial drug design and cancer biomarker discovery.

No model is ever complete: the iteration of real data and simulation facilitates continued evolution of more accurate, useful models.





SiViT Procedure

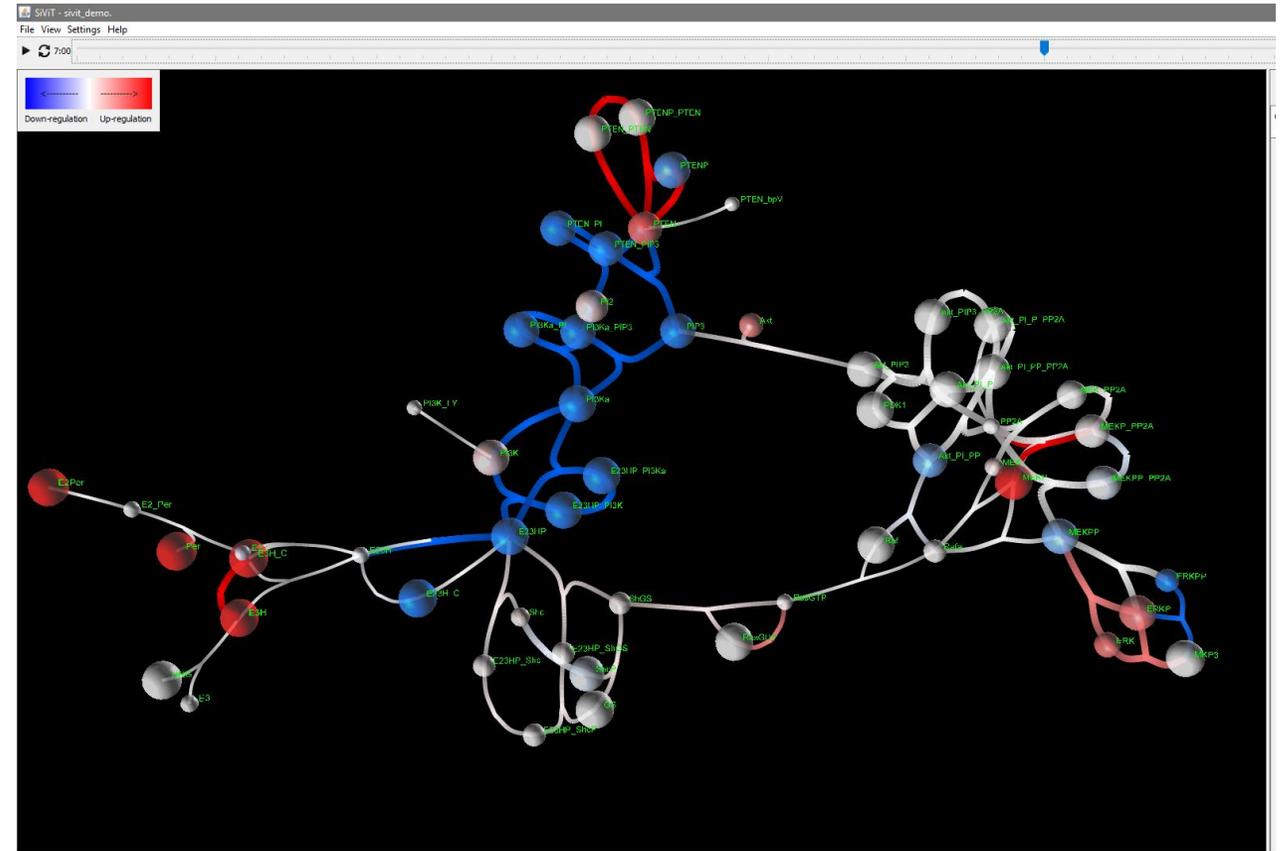
SiViT is able to load a wide range of biological models using the common mark-up language SMBL, allowing the tool to be used on a large range of cell networking investigations.

The loop between the Compute model and the Visualisation Interface is the core of SiViT allowing bi-directional communication of the model and visual interface. This allows the introduction of drugs and cancer-causing mutations that instantly update the model and display the changes in model state visually.

Visualisation

SiViT facilitates comparison of model dynamics between two different experimental regimes, for example with and without an anti-cancer drug and/or with specific mutation, through an easy-to-use menu system. Comparisons between experimental regimes are depicted using intuitive, color-coded animations. The result is an interactive exploration and discovery platform to enable the life scientist to explore and exploit existing SBML-format models of cellular signalling and drug action.

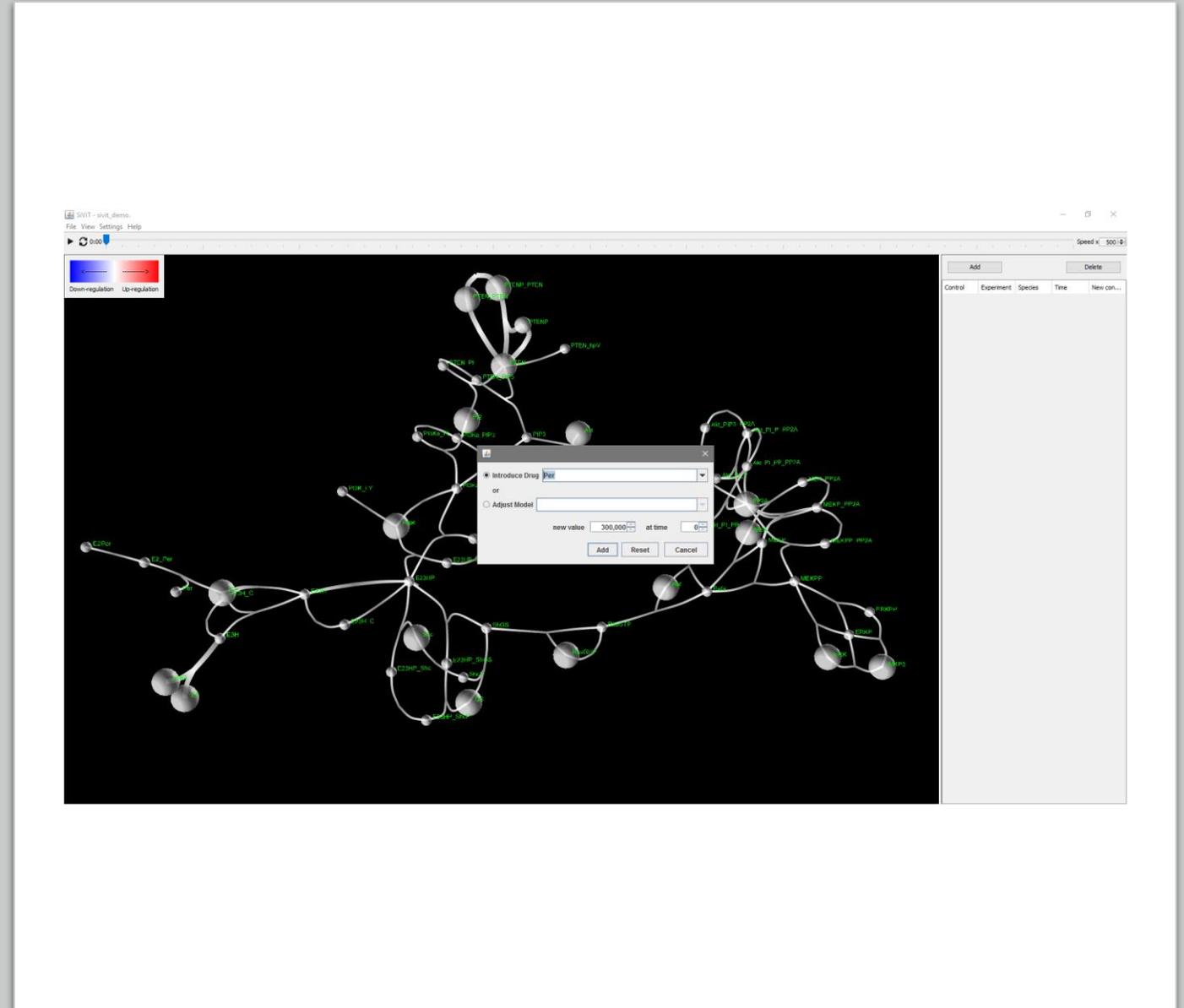
The red and blue pathways display areas of change (up and down regulation respectively), highlighting how the cell network reacts to treatment or as a comparison of cell functioning between different mutations.



Drug therapy

SiViT allows for anti-cancer drugs, alone and in combination, and cellular mutations to be applied to the system together or in sequence which is important for understanding combination therapy design. From the pop-up menu, the user can select the pre-defined drugs (at a prescribed concentration) or select a specific element of the network to mutate.

The computational model is updated and re-run with the visualisation animating the changes over time. Such modelling is useful for drug discovery since it allows rapid iteration of experimental design at low cost, before proceeding to expensive laboratory trials.



Graph

The user can select specific nodes or edges in the network and the tool generates a pop-up graph displaying the time-course data for that specific element of the network. The graph highlights the changes in concentration over time for both experimental regimes being studied (green and black lines on the graph). In this way it is possible to investigate the effect of drugs or changes on each element of the cell network over time.

