



# THE WHITE ROSE GRID

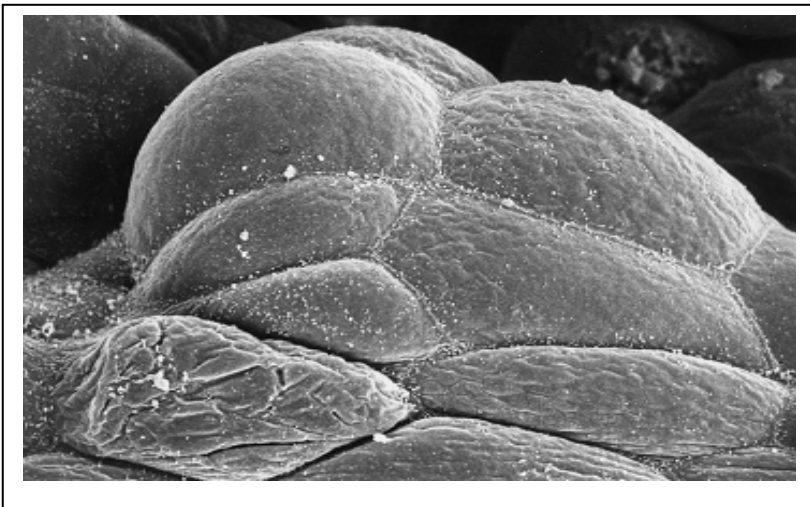
## e-Science Centre of Excellence

## Epitheliome: Predicting the social behaviour of cells in epithelial tissues

### Introduction

The aim of the Epitheliome Project is to develop a computational model that is able to predict the social behaviour of cells in epithelial tissues.

Epithelial tissues form the barriers between us and the outside world - our skin, the lining of all our body cavities (mouth, lungs, cervix, bladder, prostate gland, our intestines). They are very thin - typically about 0.5 mm thick, perhaps 10 cells - but have specialised functions. Key to epithelial behaviour is the protective barrier function



coupled with enormous repair potential. Thus skin prevents us dehydrating and protects us from disease organisms, the bladder epithelium (the urothelium) is watertight and prevents urine damage or contamination of circulating blood, the lining of our intestines protects us from potentially damaging ingested material (eg bacteria) while selectively absorbing nutrients. It is not surprising given the role of epithelia and their proliferative potential that all cancers, other than those originating from haemopoietic and mesenchymal cells, originate in epithelial tissues, which are relatively simple.

Epithelial tissues are obviously important - we can't live without them! They are also relatively simple - they contain a limited number of different cell types, no blood vessels, no nerve endings. They are the source of important clinical problems - cancer, wound healing, diabetic ulcers, skin graft contraction. The ultimate aim of our modelling is to better understand these problems, and thus be able to do something about them.

All the tissues in our bodies (to be more general, all multi-cellular creatures) self-assemble. The 'rules' for doing this are in each cell - in the genetic material. There is no information at a higher level of organisation than the individual cell, so all the organisation in tissues and organs and organisms is an 'emergent property' of the interaction of large numbers of individual cells -  $10^{13}$  in a human. That is what we are interested in - how does this social interaction of the cells produce properly functioning and structured creatures?

### X-Machines

There is no central planning in biology, and the highest level at which information is stored and processed is the genetic material in each cell. Any properties relating to multi-cellular organisation therefore have to arise as a result of interaction of individual cells. We want to address the mechanisms which underlie the transition from single to multi-cell behaviour.

This implies that we cannot impose behaviour at a tissue level on the individual cells - the behaviour at tissue level has to be an emergent property of individual cell behaviour. The emergent behaviour has to be compatible with continuum models describing the physical environment and interactions, but should not be driven by a continuum model - if it is, it is not emergent behaviour.



Our way of approaching this is to introduce the concept of representing biological systems by a virtual replicate. A replicate is defined as a software system (a model) which incorporates a 1:1 mapping of biological entities into software agents (specifically, into X-machines).

in contrast to biological observations. This enables detailed analysis of complex cellular mechanisms and their effect on tissue.

**The X-machine enable the construction of hierarchical models and formal analysis of the mathematics underlying the model distributed amongst agents.**

Individual agents have properties analogous to those of the biological entities that they represent. The X-machine is formally defined, as a result of which the virtual replicates are also formally defined, and their performance can be formally verified.

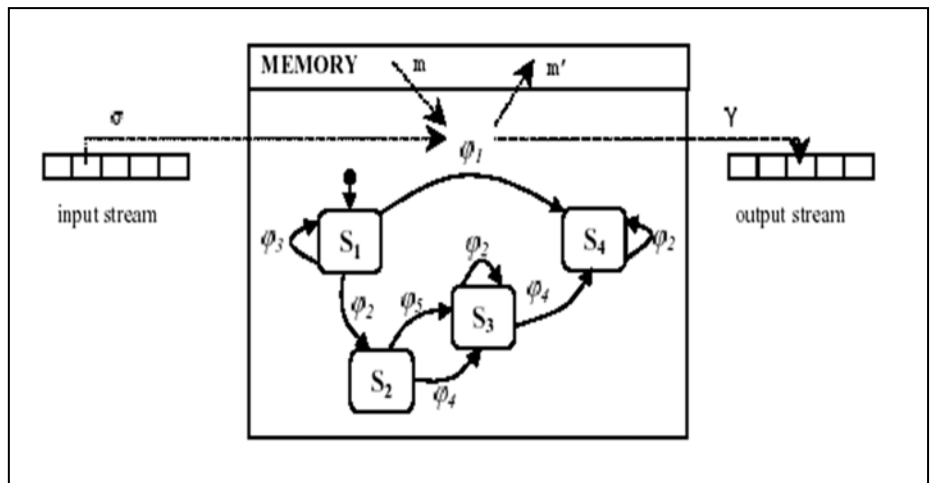
**Further Information**

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The X-machine is



Turing complete, which has two consequences:

- any function within an X-machine can be replaced by another X-machine which can evaluate the function, automatically giving rise to hierarchical models; and
- the set of functions within an X-machine could constitute a formal mathematical model thus providing a universal framework linking any type of model.

The X-machine is an inherently scalable and analytic basis upon which multi cellular models are constructed.

Having developed accurate models at the microscopic level using X-machines, simulations with many thousands of cell interaction can be performed and compared

