Complex Automata Simulation Technique

The mission of *Coast* is to develop a multi-scale, multi-science framework coined Complex Automata for modelling and simulation of complex systems based on hierarchical aggregation of coupled Cellular Automata and agent-based models.

Objectives of the project

Complex systems are typically composed of many entities whose mutual interactions produce emergent and collective behaviours. Computer simulations and rule-based modelling are often the only effective methodologies available to describe complex systems and understand or control their behaviour. Cellular Automata and Agent based models are often presented as the ideal mathematical abstraction of a complex system.

Coast will validate the Complex Automata framework by applying it to a very challenging and highly relevant biomedical application, related to treatment of coronary artery diseases

However, as many complex systems encompass many spatial and temporal scales, as well as several types of elementary components, a single, homogeneous model cannot describe them. This is the central issue that will be tackled by *Coast*. The project will address multi-scale modelling of complex systems that are made of components that act on multiple, possibly overlapping, time *and* length scales and that may involve multi-science processes.

The **main objectives of *Coast*** are to:

- Develop a multi-scale, multi-science framework coined *Complex Automata* for complex systems based on hierarchical Cellular Automata and agent based models;
- Develop a mathematical framework for Complex Automata, allowing transformation into a modelling and simulation framework;
- Identify basic ways in which information can be shared within a Complex Automaton;
- Develop a modelling and simulation software framework;
- Validate the Complex Automaton framework by applying it to a very challenging and highly relevant biomedical application, related to treatment of coronary artery disease.

Project Description

Coast is structured along three lines. First, a mathematical foundation of Complex Automata will be proposed, that should ultimately lead to a formal modelling language for Complex Automata. The main components will be: (i) a scale separation map, that places sub components of a complex automaton on the correct scales and identifies couplings, (ii) generic mechanisms for information exchange between separate scales, (iii) specification of the dynamics of the model. Second, a generic software environment will be developed for Complex Automata simulations that should allow for generic and straightforward implementation of the hierarchical coupling schemes that are part of the mathematical foundation. This software will be based on existing (agent based) distributed simulation software, which should also provide the necessary execution control structures. Thirdly, both the concept of Complex Automata and the software environment will be validated by applying it to in-stent restenosis, a very relevant multiscale problem related to Coronary artery disease. The resulting model will be validated using available in-vivo data.

A scientist wants to create a Complex Automaton model of a multi-scale complex system, such as the problem of in-stent restenosis. First, she identifies all relevant biological and physical processes, ranging from the cell cycle of individual cells, via drug elution, to bulk haemodynamics and tissue growth. These components and their interrelationships are put on a scale map to discover scale separation and to set up the final model. For each component an agent based model or a cellular automaton is taken. In some cases they already exist (for e.g. bulk haemodynamics a Lattice Boltzmann Automaton is taken), in other cases the basic models need to be developed. Using the Coast coupling framework, all components are embedded by using specific calls to coupling libraries. The whole Complex Automaton can then be executed using the Coast framework. Now the scientist starts to collect data and validate the model with in-vivo data that she has available.

Expected Results & Impacts

Our collaborative research will result in a methodology for modelling and simulation of multi-scale complex systems. Complex Automata are inherently hierarchical. ***Coast*** will define in detail the information flow between these hierarchies (using the concept of the scale separation map) and from this, extract a methodology for *model embedding* of components appearing in multi-scale Complex Automata models. The ***Coast*** simulation environment will implement a modelling language for Complex Automata. Due to the inherent hierarchical composition of Complex Automata, the simulation environment will be highly *modular*, and will express the coupling in a very generic way. Effective simulations become possible because of our scale splitting and scale separation techniques *and* the inherent distributed nature of the software. Besides these generic aspects of ***Coast***, we will apply the ***Coast*** technique to a challenging complex system arising in biomedicine. Here we will address the issue of model validation, using a large volume of (noisy and incomplete) experimental data. We will tune the subsystems in the Complex Automata model to match against these data, and use the results to build a final integrated simulation for neo-intimal growth after stenting of coronary arteries. The Complex Automata Simulation Technique that will be delivered by this project will be the foundation for innovative design strategies of complex systems in engineering. This will be demonstrated by the application that we address. The ability to model and simulate such a biomedical complex system leads the way to the next step, computer aided design of drug-eluting stents, taking full account of the multi-scale, multi-science environment in which they have to operate. In addition to the expected scientific impact, the societal impact of our application could be substantial. Coronary artery disease is the major cause of death in the Western World. The associated costs are estimated to be €45 billion Worldwide/year. Some 3 million cases of coronary artery disease are treated by stenting leading to a EU Market for these devices of >€1 billion/year. Following stenting, 5-10% of patients develop restenosis (before drug-eluting stents were introduced, this figure was 10-20%). Modelling and simulation will aid understanding of the underlying factors and lead to the development of improved drug-eluting stent technology with reduced cost and development times, and improved outcomes.

Coast

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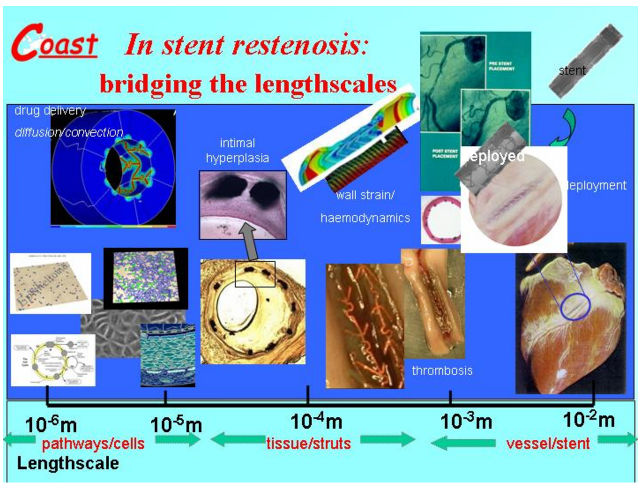
Project co-ordinator:
University of Amsterdam,
Informatics Institute,
Section Computational Science

Contact person:
Dr. A.G. Hoekstra
Tel: + 31-20-525-7543
Email: coast@complex-automata.org
Website: www.complex-automata.org



Partners:
University of Amsterdam (NL)
Technical University Braunschweig (GER)
NEC Europe Ltd. (UK)
The University of Sheffield (UK)
University of Geneva (CH)

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