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A Spatial Extension to the π Calculus

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Abstract

Spatial dynamics receive increasing attention in Systems Biology and require suitable modeling and simulation approaches. So far, modeling formalisms have focused on population-based approaches or place and move individuals relative to each other in space. SpacePi extends the π calculus by time and space. π processes are embedded into a vector space and move individually. Only processes that are sufficiently close can communicate. The operational semantics of SpacePi defines the interplay between movement, communication, and time-triggered events. A model describing the phototaxis of the Euglena micro-organism is presented as a practical example. The formalism's use and generality is discussed with respect to the modeling of molecular biological processes like diffusion, active transportation in cell signaling, and spatial structures.

Keywords: pi calculus, spatial modeling, systems biology.

1 Introduction

The majority of modeling and simulation approaches that are currently exploited in Systems Biology do not support an explicit representation and evaluation of spatial phenomena. With the progress of wet-lab techniques, spatial information becomes available that emphasizes the central role space plays in inter- and intracellular dynamics: e.g., crucial phases in the mitosis are distinguished by the spatial distribution of key actors in the cell, and signaling pathways depend on the location and movement of their components [27,26]. The relay of information in cells depends on diffusion and active transportation processes [10].

Consequently, a realistic modeling of many cellular phenomena requires that space is taken into account [10]. The modeling formalisms that have been exploited

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in Systems Biology can be distinguished along two different dimensions. One is whether the approach focuses on a population-based or individual-based perception of biological systems. The other dimension is whether a formalism allows an explicit representation of absolute space, or uses the components, their inter-relations, and their relative placement as a starting point to define space implicitly. One focus of research has been on combining absolute space and population-based approaches. E.g., partial differential equations have been used to represent signaling processes in membranes assuming a homogeneous distribution of receptors [8], and in [5] cellular automata describe the population growth of cells in space. Delays are introduced into differential equations that capture spatial phenomena implicitly, e.g. in [24] discrete time delays are used to describe transcription, translation, and nuclear transport. Thus, a population-based approach is combined with an indirect representation of space. Population-based approaches assume homogeneous distributions, which constraints their applicability, e.g. they are not suitable for realistic representations of membrane micro-domains [12]. Small numbers of actors, different geometries of components, and tracing of components causes additional problems. Furthermore, population-based approaches suffer from state space explosion [27]. This is the motivation to develop and use spatial individual-based approaches in Systems Biology. Those have so far focused on indirect, relative space. Examples are Beta Binders [20], Membrane Calculi [4] or Bio Ambients [21], which address the need to structure space into compartments and confine processes and their interactions spatially. Given the experimental set-ups, e.g. confocal microscopy, biologists are particularly interested in a combination of the individual-based approach with absolute space. Whereas some simulation systems exist that support this combination, e.g. [25,16,1], little work has so far been done with respect to modeling formalisms. We will exploit process algebras to develop a modeling formalism that allows to explicitly model location and movement of individuals in absolute space, as their use has been demonstrated in Systems Biology [18].

2 Extending the π Calculus with Space and Time

The π calculus [13] is a model of concurrent computation and is based on the notion of naming. Names represent both interconnection links between active entities, called processes, and the data that these entities exchange through communication. We extend the π calculus to allow a free movement of parallel π processes. Adding a spatial notion to a process definition is straightforward, as each process P can be associated with a certain position $\overrightarrow{p} \in V$, $V = \mathbb{R}^d$ being a vector space with a norm $\| \ \|_V$.

The introduction of movement also requires a notion of time, since the speed of motions could not be expressed otherwise. Adding time is not trivial, since we expect all communication to occur while processes are moving. Usually, a timed process algebra is built by distinguishing two phases: one in which all processes perform their actions, and one for the time to proceed [14].

Our approach expresses time by intervals and allows communication in a