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LANGUAGE DESIGN FOR COMPUTATIONAL MODELING, SIMULATION, AND VISUALIZATION

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ABSTRACT

We design BioScape, a high-level modeling language for the stochastic simulation of biological and biomaterials processes in a reactive environment in 3D space. BioScape is based on the Stochastic Pi-Calculus, and it is motivated by the need for individual-based, continuous motion, and continuous space simulation in modeling complex bacteria-materials interactions. Our models in BioScape will help in identifying biological targets and materials strategies to treat biomaterials associated bacterial infections.

The novel aspects of BioScape include high-level syntactic primitives to declare the scope in space where species can move, diffusion rate, shape, and reaction distance, and an operational semantics that deals with the specifics of 3D locations, verifying reaction distance, and featuring random movement. We dene a translation from the non-stochastic fragment of BioScape to a low-level π-calculus with 3D primitives (3π) and prove its soundness with respect to the operational semantics.

Traditionally biomaterials development consists of designing a surface and testing its properties experimentally. This trial-and-error approach is limited because of the resources and time needed to sample a representative number of configurations in a combinatorially complex scenario. Therefore, computational modeling is of significant importance in identifying best antibacterial materials to prevent and treat implant related biofilm infections.

We study bifunctional surface with polymer brushes and Pluronic-Lysozyme conjugates developed by Henk Busscher's group in Groningen, The Netherlands. The bifunctional brushes act as anti-adhesive due to the unmodified polymer brushes and antibacterial, because of the Pluronic-Lysozyme conjugates. They developed and studied three different surfaces with varying proportions of antibacterial and anti-adhesive properties. In order to aid the development of optimal bifunctional surfaces, we build a three dimensional computational model using BioScape, an agent-based modeling and simulation language. We model two different experimental phases: adhesion and growth. We use the results of experiments on two surfaces as training data, and we validate our model by reproducing the experimental results from the third surface.

The resulting model is able to simulate varying configurations of surface coatings both at adhesion and growth phases at a fraction of the time necessary to perform in-vitro experiments.
The output of the model not only plots populations over time, but it also produces 3D-rendered videos of bacteria-surface interactions enhancing the visualization of the system's behavior. We extend BioScape with a fully parallel semantics. In order to model larger and more realistic systems, a semantics that may take advantage of the new multi-core and GPU architectures motivates the introduction of Parallel BioScape, an extension with fully parallel semantics.

We present an efficient computational framework to study the large-scale bacteria-materials interactions via BioScape enabled by the massively parallel processing capability of the GPUs.

We define BioScapeL, an extension of BioScape, a Stochastic Pi-Calculus in 3D-space with abstract locations. It builds on BioScape by associating with each entity a position in space, which is the bary-center of its associated shape. The position of an entity instance is programmable. The motivation for such an extension comes from the need to describe the assembly of configurations such as polymers, oli-gomers, and complexes in space, while keeping a high level description where diffusion and confinement remain part of the semantics of the calculus. In addition to this programmable deterministic translation, we can specify random translation and scaling.

We build two models of 46 biochemical reactions in the JAK-STAT signal transduction pathway and compare the results. We implement a deterministic mathematical model using the ordinary differential equations solver COPASI, and we build a stochastic computational model using the Stochastic Pi Ma-chine (SPiM). Currently, we are working on the BioScape model of the JAK-STAT signal transduction pathway.