Spatio-Temporal Simulation Environment: a microscopy image based modelization framework

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Recently, the advancements in single cell microscopy such as fluorescent proteins (FP), used as reporters of biomolecular interactions [1], together with new image acquisition techniques (e.g. confocal [2], two-photon [3]) cause an important increase in the role of the imaging in molecular biology. These techniques open up many new areas of research - the popularization of a spatial context - to name explicitly one of the most important among them.

Currently, a common technique is to deal with images in a qualitative way - images are attached to the publications, and their properties are literally listed in the articles. A step forward from this methodology is to quantify the information from these images (e.g. the measurements of the light intensities coming from FP expressions in different parts of the cell) in a spatially resolved way. This approach has two major advantages: i) it enables us to broaden the usage of imagining techniques in systems biology, which require quantified data ii) it increases the quality of the information and allows for further automatic processing. However, this step requires dedicated software, standards and a new methodology.

Spatio-Temporal Simulation Environment (STSE) is set of *open-source* tools used to perform spatio-temporal simulations in discrete structures, based on the microscopy images. The framework contains modules to *digitize, represent, analyze*, and *mathematically model* spatial distributions of species in static and dynamic structures (e.g. growing). Digitization is performed using GUI tools allowing for user-friendly editing based on Voronoi concept [4]. STSE is freely available to the research community from `http://www.stse-software.org/`

Since the software was designed to ease the processing of biological data, it is possible to automatically acquire the information from the processed image. This information may correspond e.g. to averaged gene expression level reported by FP. It is acquired assuming that gene expression at location corresponding to pixel is proportional to the luminosity of this pixel. Then the average gene expression for a given compartment is the sum of pixel intensities belonging to this compartment divided by the number of these pixels (Figure 1b).

The example of the digitization workflow is presented in the figure 1. It is important to mention, that due to the software implementation design it is possible to relatively easily change the GUI editor behavior. As an example, this approach was used in the dynamic model of meristem growth implemented with STSE [5].

STSE is a novel tool, which is designed to ease application of the systems biology approach to microscopy data. It helps in digitization, representation, analysis, and modeling of spatial distributions of species. It conceptually differs from selection-based tools (like ImageJ [6] or Photoshop) by operating on abstract compartments rather on pixels directly. However, this approach reduces information (each compartment contains averaged information about its enclosed pixels), it results in the i) simplification of further processing (e.g. querying for image properties, building spatial models) ii) precision in defining object and properties of study iii) repeatability of measurements.

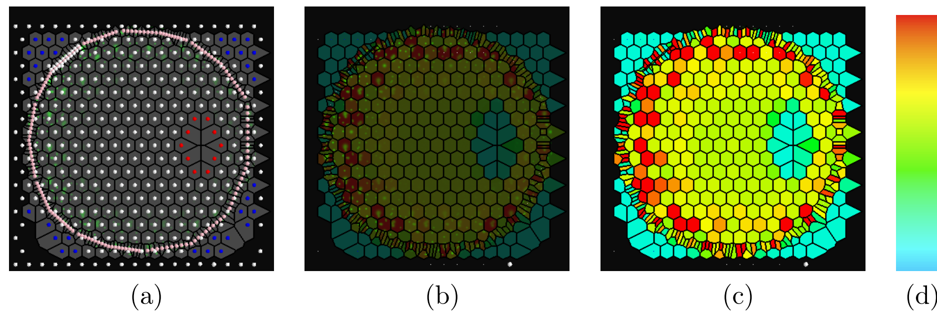

Figure 1: STSE workflow. (a) A mesh was edited by adding/moving the compartment centers. While this process, the geometry of the compartment is constantly self adjusting according to Voronoi concept. Additionally, a special property, compartment type, is depicted with the color of the sphere placed in the center of each compartment. These types may correspond e.g. to different cell objects like cytoplasm, nucleus, etc. and be used later in the analysis (e.g. to compare the average concentration of certain substance in cytoplasm with the one in the nucleus). (b) measuring the expression level based on the FP luminosity from the image placed below the mesh. The expression level is depicted by applying color gradient to the polygons of the semi-transparent mesh. (c) expression map, after removing transparency (d) color scale used to depict expression level, red values are the highest.

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