HARVARD MEDICAL SCHOOL

Faculty of Bioscience Engineering
Masters of Bioinformatics
Integrated Bioinformatics Project, 2022 - 2023

KU LEUVEN

Goo: A Python-based Blender simulation package for modeling multicellular biological tissues in 3D

Jiangli Gui[1], Julie De Man[1], Nenghan Lin[1], Vanshika Bidhan[1]| Supervisors: Antoine A. Ruzette[1,2], Prof. Sean Megason[2]
[1]Faculty of Bioscience Engineering, KU Leuven, [2]Department of Systems Biology, Harvard Medical School

Background

Simulating biologically realistic yet computationally efficient cells in a tissue environment remains a challenge in 3D. Goo, a Python-based Blender extension, is meant to fill a void in currently available models such as vertex and particle-based models, which are too simplified to capture essential features of cells and are often 2D and not user-friendly. Blender was found to be a powerful tool for biology when used to model molecular signaling in a subcellular microenvironment[1] and to visualize protein structures[2]. Goo thus provides a playground for biologists to simulate growing, self-replicating and adhering cells in biological tissues. Here, it was used to simulate the first divisions of cleaving zebrafish embryos, starting with a single blastomere on top of a yolk up to the eight-cell stage.

Software Architecture

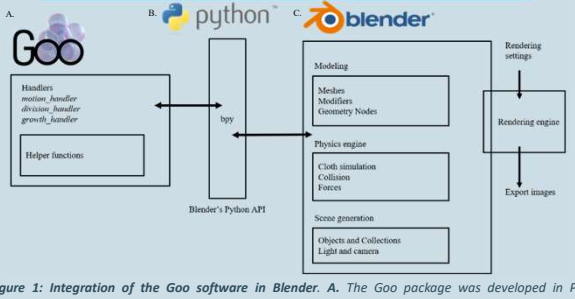

Figure 1: Integration of the Goo software in Blender. A. *The Goo package was developed in Python. Blender's handlers wrap helper functions to update the scene at every frame.* ***B.*** *Blender's Python API exposes Blender source code.* ***C.*** *Goo uses the following core Blender modules: modeling, physics, scene and objects, and rendering. A scene is made of modeled objects like meshes and forces. The scene is animated using the built-in physics engine. The rendering engine ultimately exports the scene as images or videos.*

Design and Implementation

Cell-like objects

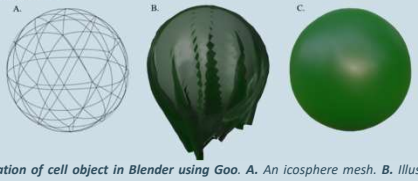

Figure 2: Creation of cell object in Blender using Goo. A. *An icosphere mesh.* ***B.*** *Illustration of the cloth modifiers enveloping the cell mesh. (This step does not actually happen in Blender)* ***C.*** *Biological cell object with green material in Blender. The mesh surface is smoothened by adding the subdivision surface modifier.*

Cell adhesion

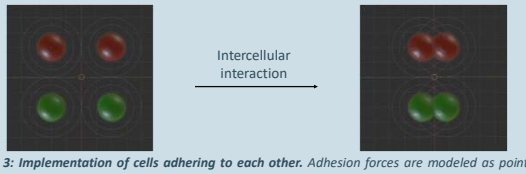

Figure 3: Implementation of cells adhering to each other. *Adhesion forces are modeled as point forces which act at the center of mass of the cell. Cells are modelled as a mesh with 'Cloth' which makes the cell responsive to physics such as forces and collisions. Cloth parameters like tension, compression, bending, etc., are optimized such that upon a collision between two cells, a force equilibrium is reached, and the cells adhere to each other. Cells of different types (cfr. green and red) will not be influenced by each other.*

Cell division

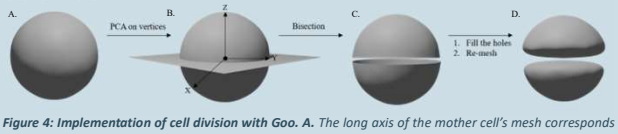

Figure 4: Implementation of cell division with Goo. A. *The long axis of the mother cell's mesh corresponds to the eigenvector of the third principal component calculated on its vertices' location.* ***B.*** *The division plane is defined by a plane orthogonal to the long axis and passes through the mother cell's center of mass. The mother cell is bisected through this division plane.* ***C-D.*** *The two newly created daughter meshes are repaired to fill the hollow structure and then re-meshed into spherical objects. The growth of daughter cells is governed by volume, and a growth rate of 1.01 that is adopted here results in a 1% increase in volume.*

Results

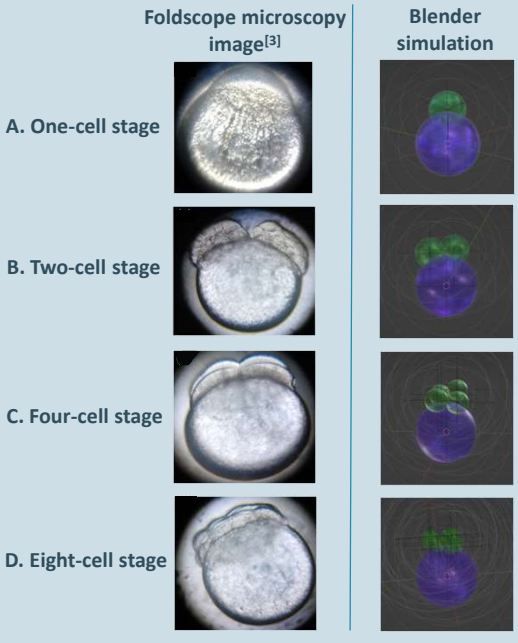

Figure 5: Comparison between real-life zebrafish embryonic development stages visualized using a foldscope microscope and Blender simulations using Goo. A-D. *Comparison between the one-cell stage, two-cell stage, four-cell stage and eight-cell stage (left) and their respective Blender simulations (right). In the Blender simulations, the yolk cell is indicated in purple, whereas the blastomeres are colored in green. Figure adapted from [3].*

Limitations

The Goo package however has some limitations. The distribution of vertices of the daughter cells after division is uneven and thus, the vertices need to be relocated. The current version of Goo still requires some optimization in terms of the division process, as in the current simulation, the division axes can only be accurately defined for the first three divisions. Forces in Goo are by default point forces which act at the center of the cell. This is a limitation because adhesion forces should be applied to the surface or the vertices of a cell object.

Future Directions

Goo has the potential to model many other biological processes. Goo can be expanded to simulate subsequent stages of zebrafish embryonic development, and to ultimately develop a 'Digital Fish'. It can also be used to track single cells during development, simulate other biological tissues, or model interactions between cells in specific environments. Thus, Goo can act as a valuable tool in the study of cell geometry, embryogenesis, morphogenesis, tissue patterning, tissue organization, tissue engineering and scientific communications.

GitHub

References

[1] Gupta, S., Czech, J., Kuczewski, R., Bartol, T. M., Sejnowski, T. J., Lee, R. E., & Faeder, J. R. (2018). Spatial stochastic modeling with MCell and CellBlender. *arXiv preprint arXiv:1810.00499.*
[2] Andrei, R. M., Callieri, M., Zini, M. F., Loni, T., Maraziti, G., Pan, M. C., & Zoppè, M. (2012). Intuitive representation of surface properties of biomolecules using BioBlender. *BMC Bioinformatics, 13*(4), S16–S16.
[3] Yesudhason BV, Cristyraj JRSS, Ganesan M, Chelladurai KS, Venkatachlam S, Ramalingam A et al. Developmental stages of zebrafish (*Danio rerio)* embryos and toxicological studies using foldscope microscope. Cell Biol. Int, 2020;44:1968–1980.