**Introduction**

The start date of the project was July 1st 2012. The project's initially planned duration was 3 years, which was extended twice (no additional funding) for a total of 2 more years. The summary below follows the list of items at the webpage http://hal.elte.hu/fij/otka of the current project. The initial goal of the project was to build on my 12 month visit (Illés Farkas, project PI) at the Center of Systems and Synthetic Biology of the University of California San Francisco (UCSF), in the groups of the PIs Wendell Lim and Chao Tang. During this preparatory visit I worked on two topics: (i) modeling the dynamics of signaling circuits, (ii) modeling how cell polarization may lead to cell aggregation during the uni-multicellular transition. Also, I arranged for Mihály Koltai – an M.Sc. student whom I was advising at that time – to visit for 2 months.

**Description by year**

During ***Year 1*** of the project I assembled and implemented a computer model of aggregating cells with the goal to describe how in unicellulars with many possible phases (single cells, chains of cells, several aggregated types) [Dayel 2011] a single aggregated phase could be amplified due to simple, biologically plausible interactions among the cells. Please see the model and the video for the project's first year at http://hal.elte.hu/fij/otka. Also during this year, the project's student participant (M. Koltai) received an outstanding offer from Heidelberg, so he left the project. During the same year I started calculations to assemble a "periodic system" of biochemical circuit functions, with the goal to extend previous work [Ma 2009] by W. Lim and C. Tang (my PIs at UCSF). Due to the lack of sufficiently interesting results and a lack of further interest from the collaborators, this remained a manuscript (see also the above webpage).

During ***Year 2*** of the project I tried to find results interesting enough to be publishable in two other directions. First, still trying to collaborate with a postdoctoral researcher (L. Morsut) of the Lim lab (UCSF) I implemented an interactive model of interactive cells undergoing polarization. The model extends the Lim lab's previous published work [Chau 2012] by considering not only a single cell, but a row of interacting cells, each containing surface regions described with the same tunable small biochemical network. During the same year a new M.Sc. student, Jeromos Kun joined the project. Based on (at that time) recent work of the Lim lab [Pincus 2008] regarding sequence domain occurrences and my previous experience with protein-protein association networks [Farkas 2015], I suggested to Jeromos to test whether the sequence-based domain predictions (all domains, not just the tyrosine kinase related domains) of the current descendants of early multicellular organisms show a domain composition different from that of unicellulars. In addition, Jeromos tested the network of domain co-occurrences in search for irregularities. Unfortunately, we have found no sufficiently novel results in this direction.

During ***Year 3*** Jeromos Kun wrapped up his work on protein domain co-occurrence changes through the unicellular-multicellular transition by assembling a "Methods" section for a planned manuscript. Later, during ***Year 4*** he presented his work at the FEBS3+ conference. Due to the lack of sufficiently interesting results that we could publish, I have decided to return to a previous direction that I had earlier pursued. In ***Years 3 to 5*** I have extended the model of Jeromos Kun's M.Sc. thesis work to a comprehensive analysis of a 2d and 3d collective motion model that provides a possible explanation for how interacting self-propelled agents can achieve large-scale aligned motion in the absence of explicit alignment [Vicsek 1995]. This direction of research has finally lead to one publication in *Physical Review E* in ***Year 3*** and one manuscript that is currently (after the end of the project's ***Year 5***) under review at *PLoS ONE*. Moreover, I presented these results at a specialized small international workshop at Uppsala University, Sweden.

**Summary**

Regarding the initial work plan, partial results have been achieved, which are available at the webpage http://hal.elte.hu/fij/otka. In a different field, there is one publication in *PRE* and one manuscript under review at *PLoS ONE*.

## References

[Dayel 2011] See Figure 2 on Page 16 of the PDF at http://goo.gl/ZaeLGQ. Dayel et. al., Cell differentiation and morphogenesis in the colony-forming choanoflagellate *Salpingoeca rosetta*. *Developmental Biology* **357**:73 (2011).

[Ma 2009] See Figure 6 on Page 770 of the PDF at http://goo.gl/eXaZkK. Ma et. al., Defining Network Topologies that Can Achieve Biochemical Adaptation. *Cell* **138**:760 (2009).

[Chau 2012] See Figure 1 on Page 321 of the PDF at http://goo.gl/tDQ5TS. Chau et. al., Designing Synthetic Regulatory Networks Capable of Self-Organizing Cell Polarization. *Cell* **151**:320 (2012).

[Pincus 2008] See Figure 2 on Page 9682 of the PDF at http://goo.gl/gnKBdb. Pincus et. al., Evolution of the phospho-tyrosine signaling machinery in premetazoan lineages. *PNAS* **105**:9680 (2008).

[Farkas 2015] A big portion of my thesis for the D.Sc. (Doctor of Science) at the Hungarian Academy of Sciences contains work on protein-protein (gene-gene) association networks that are largely sequence similarity based. The thesis summarizes work starting 2001. It can be viewed (in Hungarian) at http://real-d.mtak.hu/825.

[Vicsek 1995] Vicsek et. al., Novel Type of Phase Transition in a System of Self-Driven Particles. *Physical Review Letters* **75**:1226 (1995), https://doi.org/10.1103/PhysRevLett.75.1226.