MODELING GAP GENE EXPRESSION DYNAMICS IN A FRUIT FLY EMBRYO UNDER DIFFERENT MORPHOGEN DOSAGES

Kozlov K.N., Svichkarev A.V., Gursky V.V., Kulakovskiy I.V.[1], Surkova S.Y., Samsonova M.G.

Peter the Great St. Petersburg Polytechnic University, St. Petersburg 195251, Russia,
[1]Engelhardt Institute of Molecular Biology, RAS, Moscow, 119991, Russia
[2]Ioffe Institute, St. Petersburg, 194021, Russia

Bicoid (Bcd) as a classic morphogen plays a key role in the expression of segmentation genes in *Drosophila* embryo. The segmentation gene network controls the determination of the fruit fly segments during the blastoderm stage, just before the onset of gastrulation. We applied the systems-level approach to understand the spatial dynamics of gap gene expression domains under different Bicoid dosages using the data on the *hb* anterior domain shifts.

We obtained new parameters of the sequence-based model [1, 2] that uses thermodynamic approach to describe the target gene expression at the RNA level and two sets of reaction-diffusion differential equations for mRNA and protein concentrations to describe the dynamics of the system. The gap gene network consists of 4 gap genes – *hb*, *Kr*, *gt*, and *kni* – under control of 12 transcription factors (TF) – the products of *hb*, *Kr*, *gt*, *kni*, *bcd*, *tll*, *cad*, *hkb*, *cic*, *slp*, and *run* genes and pioneer factor Zelda. We predicted TF binding sites in the potential regulatory region from 12Kbp upstream to 6Kbp downstream of transcription start site for each gene using enhanced dinucleotide positional weight matrices. The unknown model parameters were obtained with the DEEP method by fitting the model solutions to both expression patterns of gap genes and data on the hb anterior domain shifts in embryos with varying Bcd concentration.

We compared the developed sequence-based model with the phenomenological model [3] that uses the reaction-diffusion differential equations and the matrix of regulatory coefficients characterizing the action of regulators on their targets. Both models successfully reproduce the characteristic features of experimental data. The sequence-based model reproduces the spatial dynamics of the *hb* anterior expression domain more precisely.

The study was supported by the RFBR grant 14-04-01522 and the ”5-100-2020” Program of the Ministry of Education and Science of the Russian Federation.

References.

1. K. Kozlov, V. Gursky, I. Kulakovskiy, A. Dymova and M. Samsonova, Analysis of functional importance of binding sites in the Drosophila gap gene network model. BMC Genomics 2015, 16(Suppl 13):S7
2. K. Kozlov, V. Gursky, I. Kulakovskiy, M. Samsonova (2014). Sequence-Based Model of Gap Gene Regulatory Network. BMC Genomics, 15(Suppl 12):S6
3. Andreev, S. A., Samsonova, M. G., and Gursky, V. V. (2015). Modeling of the Drosophila gap-gene network with the variation of the Bcd morphogen. Biophysics, 60(2), 173–180.