Design Principles of Cellular Networks

JUNGHYO JO

Multi-cellular organisms require systematic communication between cells to overcome external challenges. Endocrine cells interact to maintain energy metabolism; neuronal cells interact to achieve intelligence; and immune cells interact to remove dangerous things. These essential features in life are emerged from cellular networks, not from individual cells. Recently, we have launched the Junior Research Group entitled *Design Principles of Cellular Networks* to explore hidden principles in cellular networks.

In this article, I focus on introducing the cellular network for energy metabolism. The islets of Langerhans, embedded within the pancreas, play a crucial role in maintaining blood glucose levels constant by secreting the counter-regulatory hormones, insulin and glucagon. Persistent elevation of glucose levels is by definition diabetes, an increasingly common metabolic disease. The islet micro-organ consists mainly of endocrine alpha, beta, and delta cells. Although these cells are originated from the same progenitor, differentiated alpha and beta cells play opposite roles: at low glucose levels, alpha cells secrete glucagon to increase glucose levels, while at high glucose levels, beta cells secrete insulin to decrease glucose levels. It seems that two counter-regulatory components are sufficient to control (increase/decrease) glucose levels. The role of somatostatin-secreting delta cells for glucose homeostasis is still a mystery.

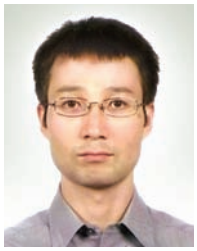
Accumulated evidence shows that these endocrine cells interact. Considering the cellular interactions within a single islet, the spatial organization of alpha, beta, and delta cells may have functional implications. Interestingly, different species have different architectures of islets for the glucose control. However, the islet size range (clusters of a few cells to several thousand cells) is similar across species having very different body sizes. In mice, beta cells are located in the islet core, while alpha and delta cells are located on the periphery. In contrast, human islets have more alpha cells (20-30% vs. 10-15% in mouse islets), and alpha and delta cells are distributed throughout islets.

In addition to the islet architecture, pieces of cellular interactions have been observed. For example, alpha cells stimulate beta cells, while beta cells inhibit alpha cells; and delta cells inhibit both alpha and beta cells. In spite of the information, the functional roles of the cellular interactions are not fully understood. We speculate that they play an important role for synchronizing hormone secretions from endocrine cells. Recent experiments with fine temporal resolution have shown that insulin, glucagon, and somatostatin secretions are pulsatile with a period of 5-10 minutes. In particular, insulin and glucagon pulses are out of phase, while insulin and somatostatin pulses are in phase. In addition to the intra-islet synchronization, the inter-islet synchronization may exist. The integrated hormone secretion from entire islets, scattered in the pancreas, also oscillates. If there was no inter-islet synchronization, asynchronous pulses from millions of human islets would compensate each other, and their averaged hormone pulse would become flat.

Patients with type 1 diabetes have insufficient beta cells because their own beta cells are destroyed in the autoimmune disease. To cure those patients, artificial pancreas has been proposed. It continuously monitors blood glucose levels, and injects insulin/glucagon whenever glucose levels increase/decrease. It has been experimentally proved that this simple strategy worked well. However, our natural glucose controller, the islet, uses pulses (instead of monotonic responses) and systematic combinations of insulin, glucagon, and somatostatin pulses.

Our group aims to understand design principles in the endocrine cell network, and provide the efficient algorithm for controlling glucose homeostasis. Furthermore, we have general interests in various biological networks and their evolution. Whoever has a strong motivation in studying computational biology is welcome to join our team:

http://APCTP.org/jrg/blogindex.php?JrgId=13.



Junghyo Jo earned his PhD in theoretical physics from Seoul National University in 2007. After postdoctoral research at National Institutes of Health, Bethesda, USA from 2007 to 2012, he joined APCTP as a leader of the computational biology group in September 2012.

[ANNOUNCEMENT]

President Position Open at APCTP

The Asia Pacific Center for Theoretical Physics (APCTP) is an international research center that pursues excellence in research, trains young scientists in all areas of theoretical physics, and promotes international cooperation among scientists from member countries/regions in the Asia-Pacific region and beyond.

The APCTP seeks exceptionally qualified candidates for the President position in areas of theoretical physics. Ideal candidates must have an active and proven record of excellence in funded research, publications, and professional service as well as a demonstrated administrative ability. In addition to developing or expanding high-quality research programs, all successful applicants must be committed to preeminence in leading the APCTP's academic activities. A successful candidate will be offered an opportunity to be jointly appointed as a distinguished professor in the Department of Physics at the Pohang University of Science and Technology (POSTECH). The APCTP aims to lead the advancement of physics by enhancing international academic collaboration. Candidates who can contribute to that goal are encouraged to apply and identify their strengths and experiences in this area.

To apply, a letter of interest and curriculum vitae should be submitted to Prof. Won Namkung, Chair of the Search Committee for President by e-mail at Namkung@postech.ac.kr.

The application review process will begin on January 1, 2013, and will continue until the position is filled.

For further information,
please contact the Chair at ***+82-54-279-1006.***