Time and spatial scales of epigenetic dynamics
エピジェネティック動力学の時空間現象

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One of the most challenging problems in cell biology is to reveal the mechanism how complex processes including assembly of transcriptional apparatus, histone modification, and organization of chromatin structures regulate the eukaryotic gene expression. Time and spatial scales of these processes are hierarchically distributed, and hence the new concepts and methods are required to analyze processes interacting across the multiple scales. We address this problem by theoretically investigating the eukaryotic gene expression in two examples: One is the large phenotypic heterogeneity of ES cells. By modeling the network of epigenetic gene switches of mouse ES cells, we show that the slow switching of *Nanog* due to the large reorganization of chromatins should be the origin of the large phenotypic heterogeneity of ES cells. We quantitatively draw epigenetic landscapes to describe the simulated differentiation process from ES cells, and show that the large fluctuation of ES cells due to the slow *Nanog* switching helps the stable differentiation. Another example is the fluctuating dynamics of genome structure of budding yeast. We constructed a model of genome dynamics by using the Hi-C data and simulated the fluctuating motion of chromosomes in interphase nucleus (Fig.1). We examine the possibility that genes are regulated both in activating and repressing ways through the spatial distribution of genome in nucleus.

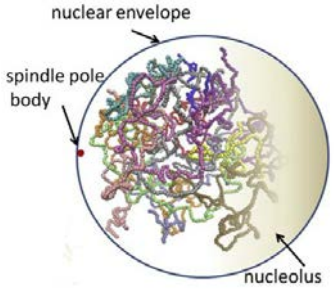

Fig.1 A snap shot of the dynamical simulation of genome structure of interphase nucleus of budding yeast.

References

1) Masaki Sasai, Yudai Kawabata, Koh Makishi, Kazuhito Itoh, and Tomoki P. Terada (2013) Time scales in epigenetic dynamics and phenotypic heterogeneity of embryonic stem cells. *PLoS Comp. Biol*. **9**: e1003380.
2) N. Tokuda, T. P. Terada, and M. Sasai (2012) Dynamical modeling of 3D genome organization in interphase budding yeast. *Biophys. J.* **102**: 296-304, Correction **102**: 719-719.