Visualizing the appearance and disappearance of the attractor of differentiation using Raman spectral imaging

Taro Ichimura, Liang-da Chiu, Katsumasa Fujita, Hiroaki Machiyama, Satoshi Kawata, Tomonobu M. Watanabe & Hideaki Fujita

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Using Raman spectral imaging, the research groups of Tomonobu Watanabe (RIKEN QBiC) and Hideaki Fujita (Single Molecule Imaging, IFReC) visualized the cell state transition during differentiation and constructed hypothetical potential landscapes for attractors of cellular states on a state space composed of parameters related to the shape of the Raman spectra. As models of differentiation, they used the myogenic C2C12 cell line and mouse embryonic stem cells. Raman spectral imaging can validate the amounts and locations of multiple cellular components that describe the cell state such as proteins, nucleic acids, and lipids; thus, it can report the state of a single cell.

The groups visualized the cell state transition during differentiation using Raman spectral imaging of cell nuclei in combination with principal component analysis. During differentiation, cell populations with a seemingly homogeneous cell state before differentiation showed heterogeneity at the early stage of differentiation. At later differentiation stages, the cells returned to a homogeneous cell state that was different from the undifferentiated state. Thus, Raman spectral imaging enables us to illustrate the disappearance and reappearance of an attractor in a differentiation landscape, where cells stochastically fluctuate between states at the early stage of differentiation.

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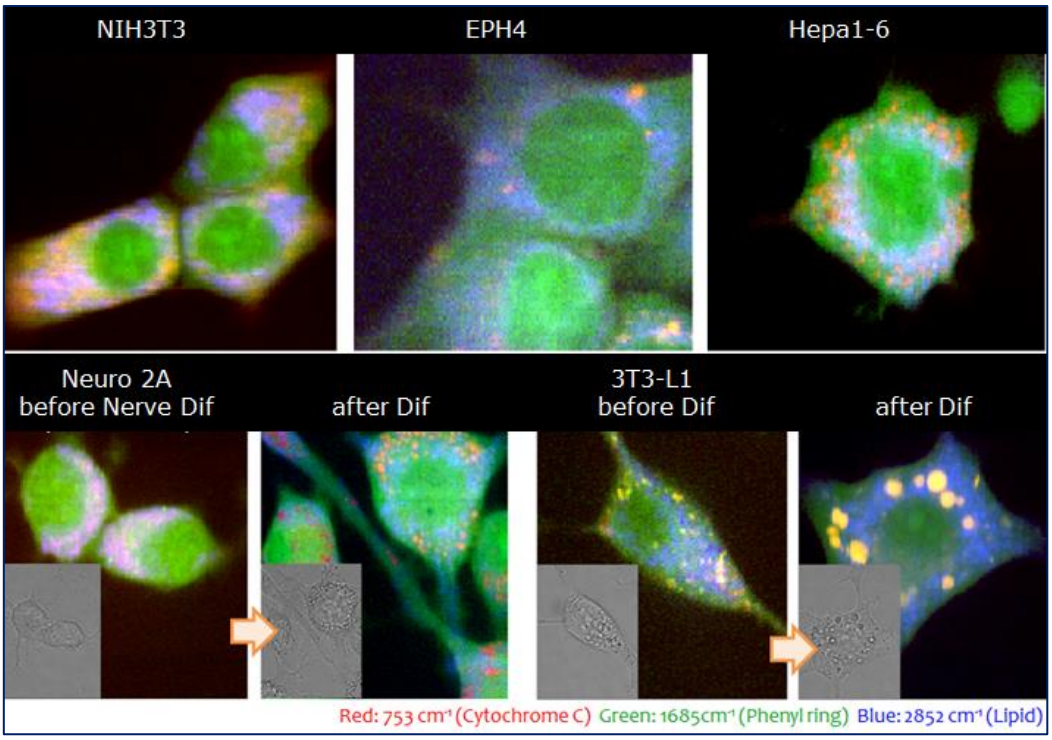
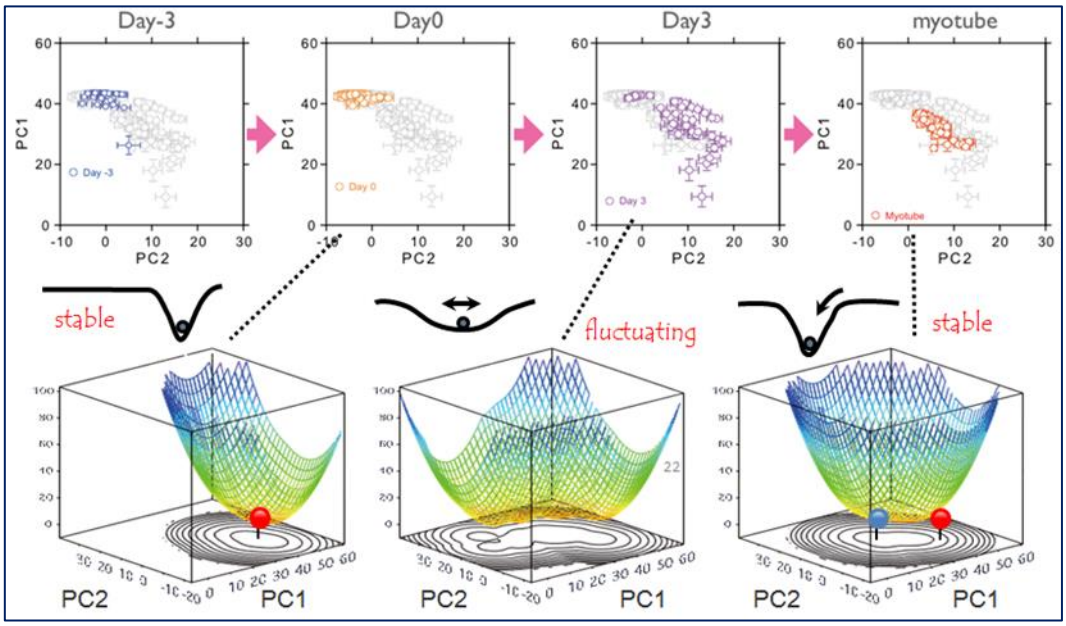


Each color in the cell represents the difference of the Raman spectra. The colors of the cytoplasm and cell nucleus depend on the type of cells or on the stage of cell differentiation.



The potential landscapes in cell differentiation using Raman spectral imaging