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Single-cell entropy for quantifying differentiation potency of normal and cancer stem-cell phenotypes

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60 years ago Conrad Waddington proposed his famous epigenetic landscape to model cellular differentiation. 60 years later, we still do not have a convincing theoretical framework for constructing these epigenetic landscapes. For instance, using molecular profiles of a cell (e.g. RNA-Seq) we are still unable to quantify the differentiation potential of a cell in this landscape. This presentation reports our progress in quantifying differentiation potential of a single cell from its genome-wide RNA-Seq profile. Specifically, we proposed to quantify differentiation potential by computing the signaling entropy rate of a diffusion process on an integrated network specified by a stochastic interaction matrix. Using RNA-Seq data from over 7,000 single cells we showed that signaling entropy is able to discriminate with very high accuracy pluripotent from multipotent and terminally differentiated cells without the need for model training or feature selection. We further show that signaling entropy is a more robust measure of differentiation potency than other entropy-based measures, driven in part by a subtle positive correlation between the transcriptome and connectome. Signaling entropy is able to identify known subpopulations of varying potency as well as drug resistant cancer stem-cell phenotypes, including those derived from circulating tumor cells. In summary, signaling entropy provides an *in silico* measure of differentiation potency that works for both single cells and bulk samples and may provide a means to identify normal and cancer stem-cell phenotypes.

Biography

Andrew Teschendorff is a Professor of Computational Systems Genomics at the CAS-MPG Partner Institute for Computational Biology, Shanghai, China, as well as a Royal Society Newton Advanced Fellow and Principal Investigator at University College London, UK. He has obtained his PhD in Mathematical Physics at Cambridge University, UK. He has completed his academic posts at the University of Warwick and Cambridge University. His research is the interface between statistical modeling, systems biology and cancer epigenomics with a particular focus on understanding the role of epigenetic variation in ageing and cancer.

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