Abstract Submitted
for the MAR14 Meeting of
The American Physical Society

Epigenetic landscape of master regulators with cooperative feedback ANDREAS KRAEMER, Ingenuity Systems, Inc. — A common view is that cell phenotypes can be understood as attracting valleys in a complex epigenetic landscape. On the other hand, cell fates have also been associated with master regulatory genes controlling development, which is particularly important in the context of cellular reprogramming. In this work I describe a simple noisy model of gene regulation in which master transcription regulators are involved in cooperative positive feedback loops with a large number of downstream regulated genes. It is shown that this model can be mapped onto a finite-temperature Hopfield associative memory spin model with effective pairwise Hebbian interactions, thus providing a mechanism for concurrent storage of gene expression patterns representing different cell states, where each cell state is associated with a particular master regulator. The inclusion of simple dynamics then leads to a description in terms of an N-dimensional potential landscape, N being the number of regulators. Within this model I discuss the stability of cell states as well as different mechanisms of switching between states when triggered by an external signal, suggesting possible scenarios for cell differentiation events.

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Date submitted: 15 Nov 2013 Electronic form version 1.4