REFERENCES NOTES

**Title:**

**Link:**

**Comments:**

**Title:** A new mechanism of stem cell differentiation through slow binding/unbinding of regulators to genes

**Link:** https://www.nature.com/articles/srep00550

**Comments:** Jin Wang landscape application. Two genes which repress each other and activate themselves treated in CME formalism using Gillespie simulations. P\_ss calculated via simulations, used to construct Wang landscape. Notable: example of using P\_ss landscape for non-continuous state space.

**Title:** A physical mechanism of cancer heterogeneity

**Link:** https://www.nature.com/articles/srep20679#supplementary-information

**Comments:** Jin Wang landscape application. Two genes which repress each other and activate themselves (interpreted as producing a ‘normal’ state, ‘premalignant’ state, a ‘cancer’ state, and possibly some others depending on how many attractors appear). Message: cancer heterogeneity may be a consequence of epigenetic regulation causing the timescale of protein regulation to be similar to the timescale of protein synthesis. When this happens, many new attractors appear, making it easier to reach a cancer attractor. Landscape may be useful for visualizing/understanding this. Another case of using P\_ss landscape for CME.

**Title:** Kinetic paths, time scale, and underlying landscapes: A path integral framework to study global natures of nonequilibrium systems and networks

**Link:** https://aip.scitation.org/doi/10.1063/1.3478547

**Comments:** Jin Wang used his (wrong!) path integral to study the phage lambda genetic switch. They also developed the formalism a little. Contains many refs (see 11-18) to years of previous path integral-related work.

**Title:** Quantifying Cell Fate Decisions for Differentiation and Reprogramming of a Human Stem Cell Network: Landscape and Biological Paths

**Link:** https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1003165

**Comments:** Jin Wang landscape application. Used landscape to study 52 gene stem cell network. Langevin dynamics used (state space is huge, after all).

**Title:** A landscape view on the interplay between EMT and cancer metastasis

**Link:** https://www.nature.com/articles/s41540-018-0068-x#ref-CR35

**Comments:** Non-Jin Wang app. EMT network created to study EMT/cancer metastasis using the landscape. P\_ss landscape computed. Langevin regime.

**Title:** Cancer attractors: A systems view of tumors from a gene network dynamics and developmental perspective

**Link:** https://www.sciencedirect.com/science/article/pii/S1084952109001499?via%3Dihub

**Comments:** Big opinion article by Sui Huang et al on interpreting cancer in the context of (normally) unused attractors in the landscape. Can be used as a general source for this idea in the article (interpreting cancer in terms of the landscape).

**Title:** Nanog induced intermediate state in regulating stem cell differentiation and reprogramming

**Link:** https://bmcsystbiol.biomedcentral.com/articles/10.1186/s12918-018-0552-3

**Comments:** Application of landscape to development. Nanog can help lower transition barrier for stem cells.

**Title:** A mathematical model of mechanotransduction reveals how mechanical memory regulates mesenchymal stem cell fate decisions

**Link:** https://bmcsystbiol.biomedcentral.com/articles/10.1186/s12918-017-0429-x

**Comments:** Application of landscape to development. Mesenchymal stem cells differentiate into various kinds of cells (neurons, adipocytes, myocytes, and osteoblasts) depending on their substrate’s stiffness. Used the landscape to visualize how changing stiffness changes what cell fates the stem cell is likely to turn into.

**Title:** Landscape and flux reveal a new global view and physical quantification of mammalian cell cycle

**Link:** http://www.pnas.org/content/111/39/14130

**Comments:** Jin Wang landscape application to understanding and visualizing cell cycle.

**Title:** Transition state characteristics during cell differentiation

**Link:** https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1006405

**Comments:** Relatively new article with lots of good references. Sort of discusses global vs local landscapes, and the role of the ‘curl flux’ term. Might use for local/Friedlin-Wentzell landscape references. Application to development, completely in the Langevin regime.

**Title:** Quantifying the Landscape for Development and Cancer from a Core Cancer Stem Cell Circuit

**Link:** http://cancerres.aacrjournals.org/content/75/13/2607.long

**Comments:** Jin Wang landscape application. ‘Confirms’ role of p53 in preventing transition to cancer stem cell state via model of ‘core’ cancer circuit. Langevin regime.

**Title:** Mathematical Formalism of Nonequilibrium Thermodynamics for Nonlinear Chemical Reaction Systems with General Rate Law

**Link:** http://link-springer-com-443.webvpn.jxutcm.edu.cn/article/10.1007%2Fs10955-016-1678-6

**Comments:** Explains link between phi = - log P\_ss and chemical kinetics. Basically just interesting/novel for that.

**Title:** Mesoscopic kinetic basis of macroscopic chemical thermodynamics: A mathematical theory

**Link:** https://journals.aps.org/pre/abstract/10.1103/PhysRevE.94.052150

**Comments:** Proves link between phi = - log P\_ss and chemical kinetics. Same as above, same authors as above. Include these papers at the end of the P\_ss landscape section. (The P\_ss landscape also has a novel interpretation as the free energy, as long as some mild assumptions are true.)

**Title:** Quantifying Waddington landscapes and paths of non-adiabatic cell fate decisions for differentiation, reprogramming and transdifferentiation

**Link:** http://rsif.royalsocietypublishing.org/content/10/89/20130787#sec-7

**Comments:** Human embryonic stem cells (ES) studied using the P\_ss landscape. Gillespie simulations used, so they worked in the discrete infinite regime.

**Title:** Uncovering the underlying mechanism of cancer tumorigenesis and development under an immune microenvironment from global quantification of the landscape

**Link:** http://rsif.royalsocietypublishing.org/content/14/131/20170105.full

**Comments:** Model of cancer-immune system interaction in context of tumorigenesis. P\_ss landscape used to study, Langevin dynamics used. Talk here (as in a few other Jin Wang papers) about the self-consistent mean field approximation for finding P\_ss. This basically amounts to approximating P\_ss as many superimposed Gaussians. Should probably say something about this at the end of the P\_ss landscape section.

**Title:** Landscape and flux theory of non-equilibrium dynamical systems with application to biology

**Link:** https://www.tandfonline.com/doi/full/10.1080/00018732.2015.1037068

**Comments:** Massive (137 pages!!) review authored solely by Jin Wang explaining various aspects of his P\_ss landscape. Good to present as a thorough reference on this kind of landscape. Also has many details explaining Wang’s view of path integrals applied to cell state transition paths. (I still think he is sort of wrong though.)

**Title:** A Physical Mechanism and Global Quantification of Breast Cancer

**Link:** https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0157422

**Comments:** Jin Wang application of landscape to breast cancer. Simple GRN was constructed and analyzed using P\_ss landscape. Langevin regime.

**Title:** The Potential Landscape of Genetic Circuits Imposes the Arrow of Time in Stem Cell Differentiation

**Link:** https://www.sciencedirect.com/science/article/pii/S0006349510004248#bib69

**Comments:** Application (by Jin and Sui) of landscapes to a fundamental idea of development. The idea is: given that inter-attractor transitions are in principle bidirectional, what causes development to proceed so reliably in one direction? In fancier language, what is the origin of the ‘arrow of time’?

**Title:** Exploring the Mechanisms of Differentiation, Dedifferentiation, Reprogramming and Transdifferentiation

**Link:** https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0105216

**Comments:** Review of landscape view of different kinds of differentiation in context of development and reprogramming by Wang. Good source for specifics about trans vs de-differentiation (they discuss it in the language of bifurcations). Also discuss the path integral in passing, and use the same (wrong!) one as all the other Wang papers, with the extra DEL DOT F term. Ad-hoc additive noise used.

**Title:** Engineering of a synthetic quadrastable gene network to approach Waddington landscape and cell fate determination

**Link:** https://cdn.elifesciences.org/articles/23702/elife-23702-v1.pdf

**Comments:** Application of Jin Wang P\_ss landscape to understanding a synthetic network constructed in E. coli (two genes, activating themselves and repressing each other). Jin Wang didn’t write this one! Ad-hoc additive noise with uniform noise strength D used, as in many Jin Wang papers. Synthetic bio application…should this appear in a separate section?

**Title:** Modeling the epigenetic attractors landscape: toward a post-genomic mechanistic understanding of development

**Link:** https://www.frontiersin.org/articles/10.3389/fgene.2015.00160/full

**Comments:** Solid review of some landscape ideas, kind of light on the math. Reads like it was not written by a physicist, but a biologist, because there is an emphasis on following the history of ideas. Lots of good references here.

**Title:** Stochastic Methods: A handbook for the natural and social sciences

**Link:**

**Comments:** Should cite this as solid reference for general knowledge on Langevin/Fokker-Planck/stochastic calculus.

**Title:** Attractor Landscape Analysis Reveals Feedback Loops in the p53 Network That Control the Cellular Response to DNA Damage

**Link:** http://stke.sciencemag.org/content/5/251/ra83.long

**Comments:** Non-Wang application of Wang landscape to understanding how feedback loops in the p53 regulatory network affect a cell’s response to DNA damage (related to cancer, so will probably put it in that section). Said they used a probabilistic Boolean network, and found the P\_ss for a system of discrete master equations.

**Title:** Feynman and Hibbs

**Link:**

**Comments:** Of course.

**Title:** Kleinert path integral monograph

**Link:**

**Comments:** Of course.

**Title:** Space-Time Approach to Non-Relativistic Quantum Mechanics

**Link:** https://journals.aps.org/rmp/abstract/10.1103/RevModPhys.20.367

**Comments:** Feynman’s original path integral paper.

**Title:** Quantifying the underlying landscape and paths of cancer

**Link:** http://rsif.royalsocietypublishing.org/content/11/100/20140774.full

**Comments:** Yet another Jin Wang cancer model/perspective. Model cancer network created and analyzed, turns out to be tristable: normal, cancer, apoptosis states. Langevin regime with symmetric additive noise D. Mention of the gradF path integral.

**Title:** Landscape reveals critical network structures for sharpening gene expression boundaries

**Link:** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6001026/

**Comments:** Application of P\_ss landscape to understanding the creation of sharp boundaries in developmental pattern formation. Think Li is a student of Jin’s. Langevin regime, symmetric additive noise D, 2D bistable switch.

**Title:** USE REFS 17-21 FROM WRITTEN PROPOSAL AS REFS FOR ‘gene exp is innately noisy’

**Link:**

**Comments:**

**Title:** Cell fate potentials and switching kinetics uncovered in a classic bistable genetic switch

**Link:** https://www.nature.com/articles/s41467-018-05071-1

**Comments:** Mutually repressing transcription factors in bacteriophage lambda, experimentally constructed and landscape (bistable switch with four stable states) realized. Landscape constructed experimentally!!! (but this is possible because the system is 2D) Also construct a Markov chain model. (Hidden Markov model) Maybe should search HMM and see what pops up to get refs for the Markov chain discussion.

**Title:** Path integral solutions of stochastic equations for nonlinear irreversible processes: The uniqueness of the thermodynamic Lagrangian

**Link:** https://aip.scitation.org/doi/pdf/10.1063/1.442098?class=pdf

**Comments:** See Eq. 16: looks good, get the correct result for alpha = 0 (Ito interpretation). Then the rest of the argument on pg. 978 makes a change of variables to assert that the final Lagrangian is alpha-independent (MISTAKE!). This paper was cited by a 1993 paper of Jin Wang and Wolynes.

**Title:** Potential landscape and flux framework of nonequilibrium networks: Robustness, dissipation, and coherence of biochemical oscillations

**Link:** http://www.pnas.org/content/105/34/12271

**Comments:** First Jin Wang P\_ss landscape paper? Apply to cyclin fluctuations in budding yeast cell cycle.

**Title:** Potential Energy Landscape and Robustness of a Gene Regulatory Network: Toggle Switch

**Link:** https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.0030060

**Comments:** Slightly earlier attempt than the one above to construct a landscape. P\_ss plotted here, and potential defined as P\_ss = exp(-U).

**Title:** Funneled Landscape Leads to Robustness of Cell Networks: Yeast Cell Cycle

**Link:** https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.0020147#abstract0

**Comments:** Same as above, came out just before 2008 paper “Potential landscape and flux…” and contains mention of U := -log(P\_ss). As title suggests, using landscape as tool to study robustness of yeast cell cycle.

**Title:** Potential in stochastic differential equations: novel construction

**Link:** http://iopscience.iop.org/article/10.1088/0305-4470/37/3/L01/meta

**Comments:** Ao’s original landscape construction paper. Will need to study this a bit to see where he’s coming from. Note: says in the last sentence of the article that this potential is allowed to be time-dependent. In this way, it’s different from Jin Wang’s P\_ss landscape. Is this a local landscape, according to my definition?

**Title:**

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**Comments:**

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