Interdisciplinary research: Easier said than done

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Interdisciplinarity: Easier said than done

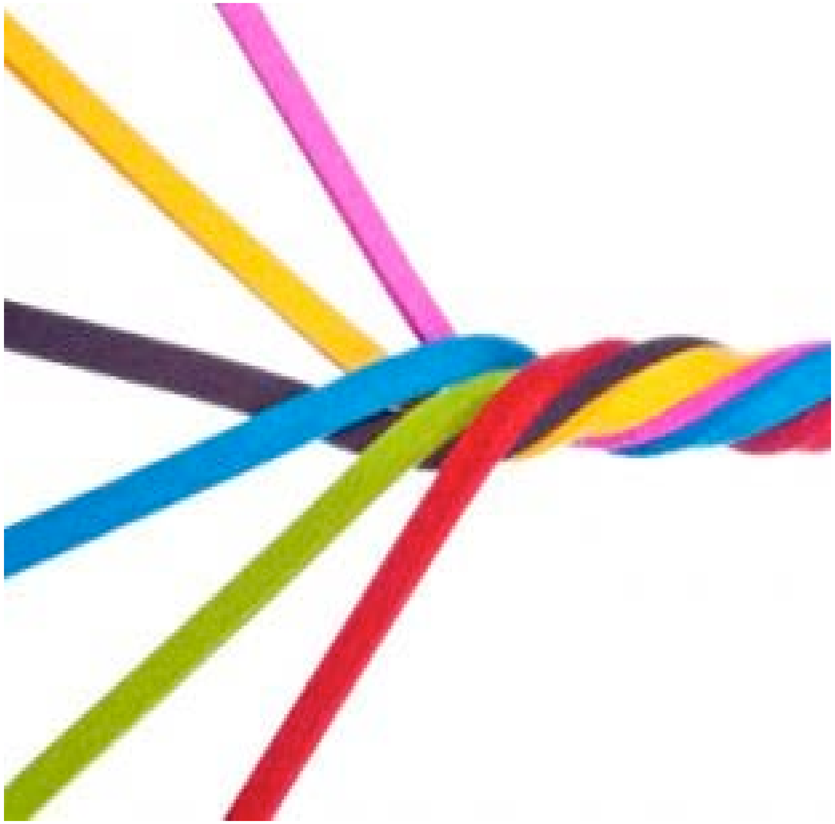
Mathematicians

Computer scientists

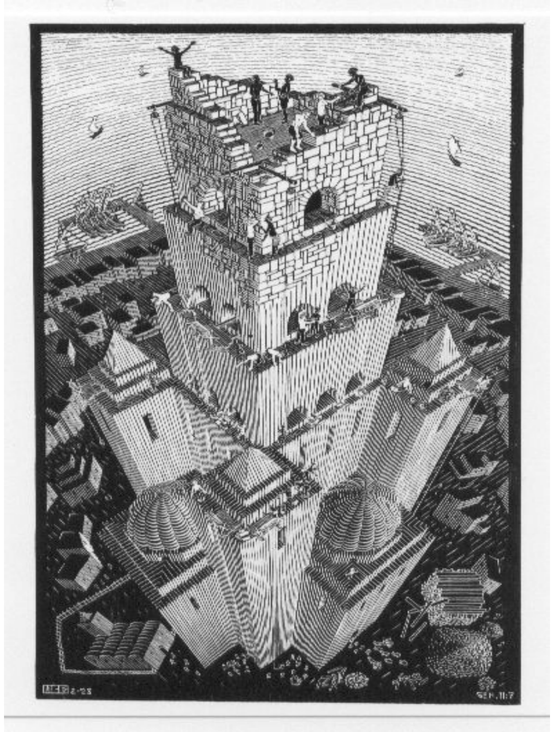
Engineers

Biologists

Chemists



Medical doctors



“The art is in the leadership”

insight commentary

Organizational challenges in clinical genomic research

Jill S. Altshuler[1] & David Altshuler[2]

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[2]*Departments of Genetics and Medicine, Harvard Medical School and Masschusetts General Hospital, and Broad Institute, 55 Fruit Street, Wellman 8, Boston, Massachusetts 02114, USA (e-mail: altshuler@molbio.mgh.harvard.edu)*

Genome sequence data are enabling clinical genomic investigation, in which the characteristics of human patients are explored using comprehensive inventories of biomolecules. Successful investigators must navigate rapid technological change, collect and analyse large volumes of data, and engage systems of clinical care. Such projects will increasingly rely on fully integrated multidisciplinary teams, demanding new organizational models in academic biomedical research.

“Put the success of the group over the success of the individual”

Interdisciplinary Teams

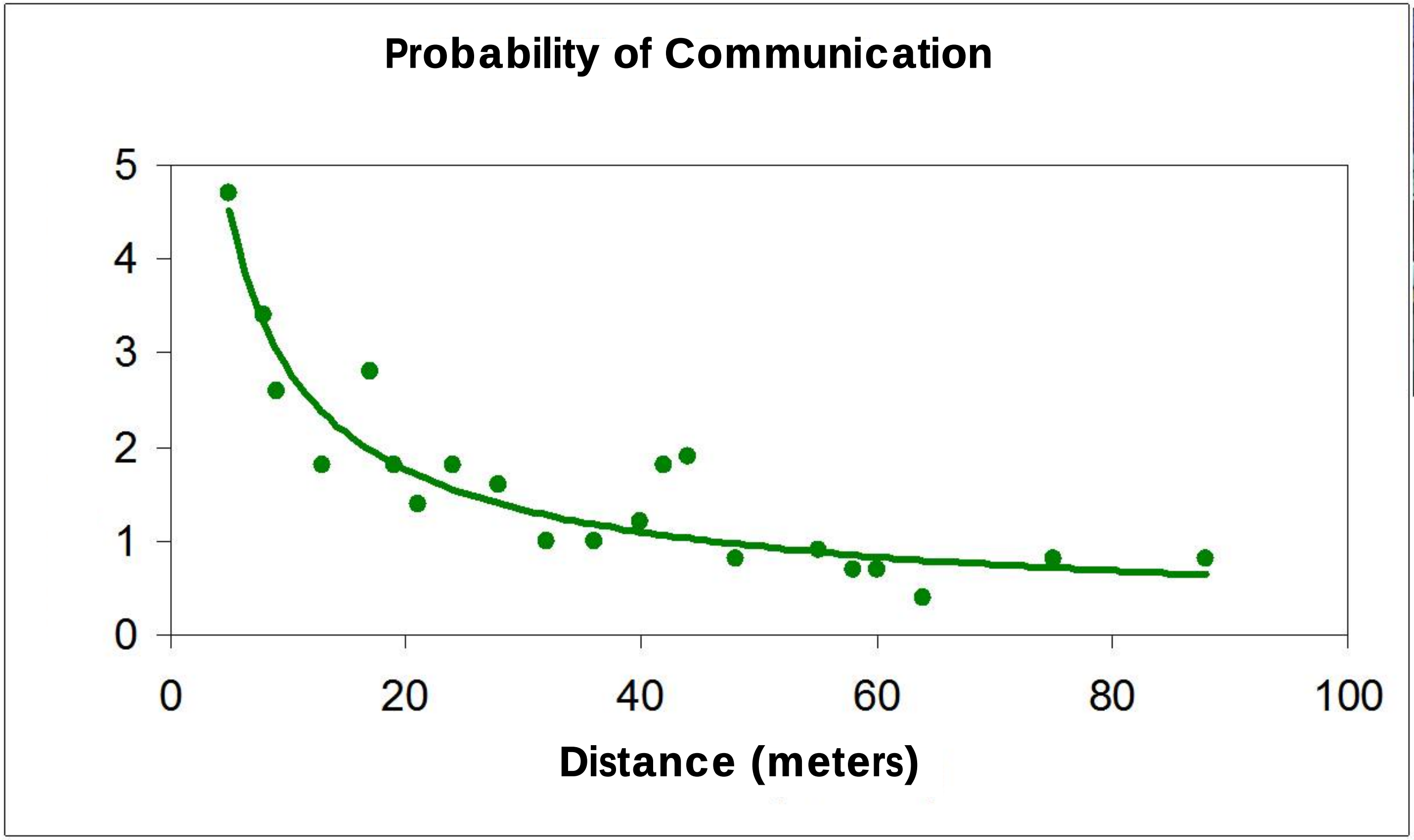
In recruiting for such teams,
disciplinary excellence is not the sole criterion.

Individuals must be flexible and open-minded,
have good communication and social skills,

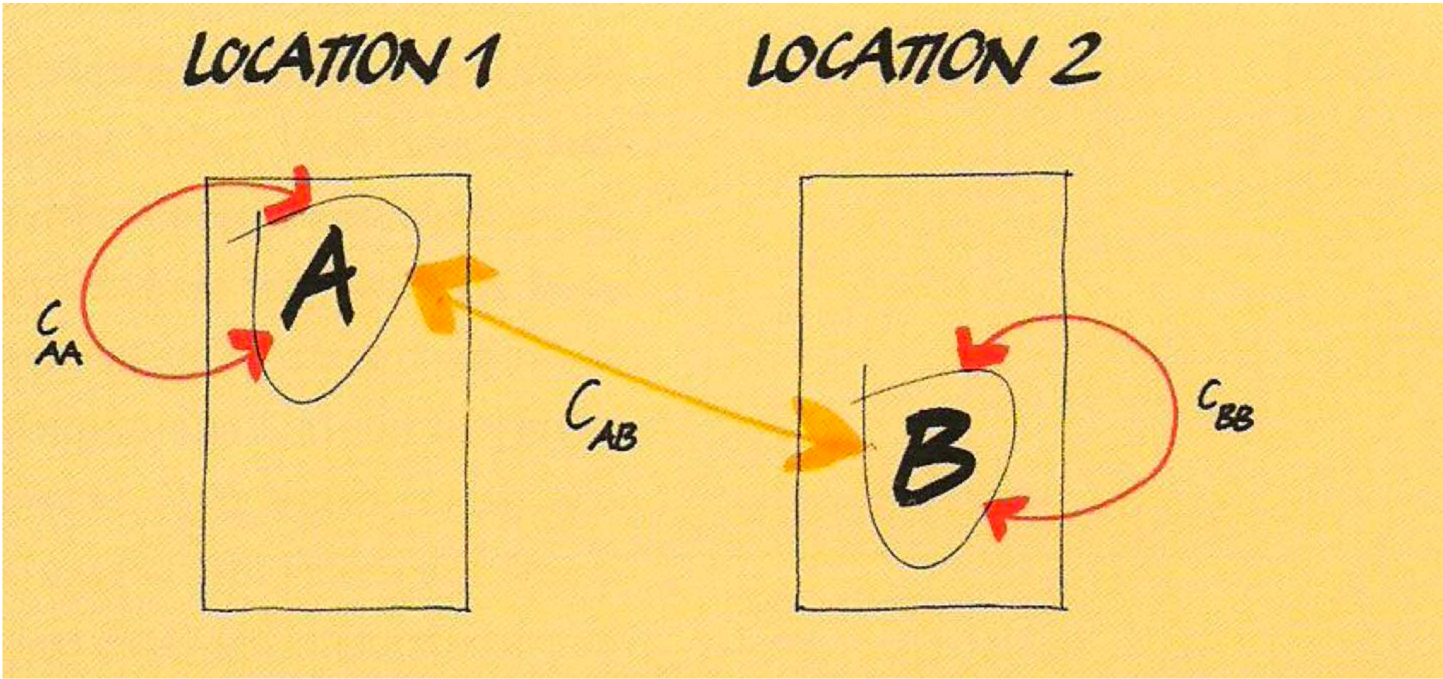
and be willing to work with others
in pursuit of a common goal.

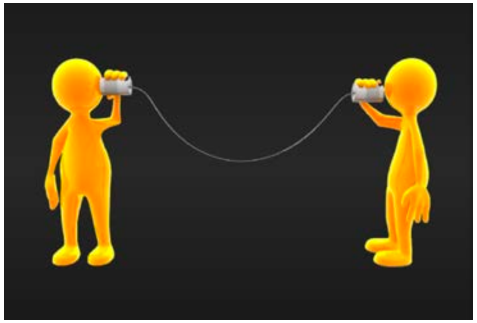
J.S. Altshuiler & D. Altshuiler 2004

Distance matters…



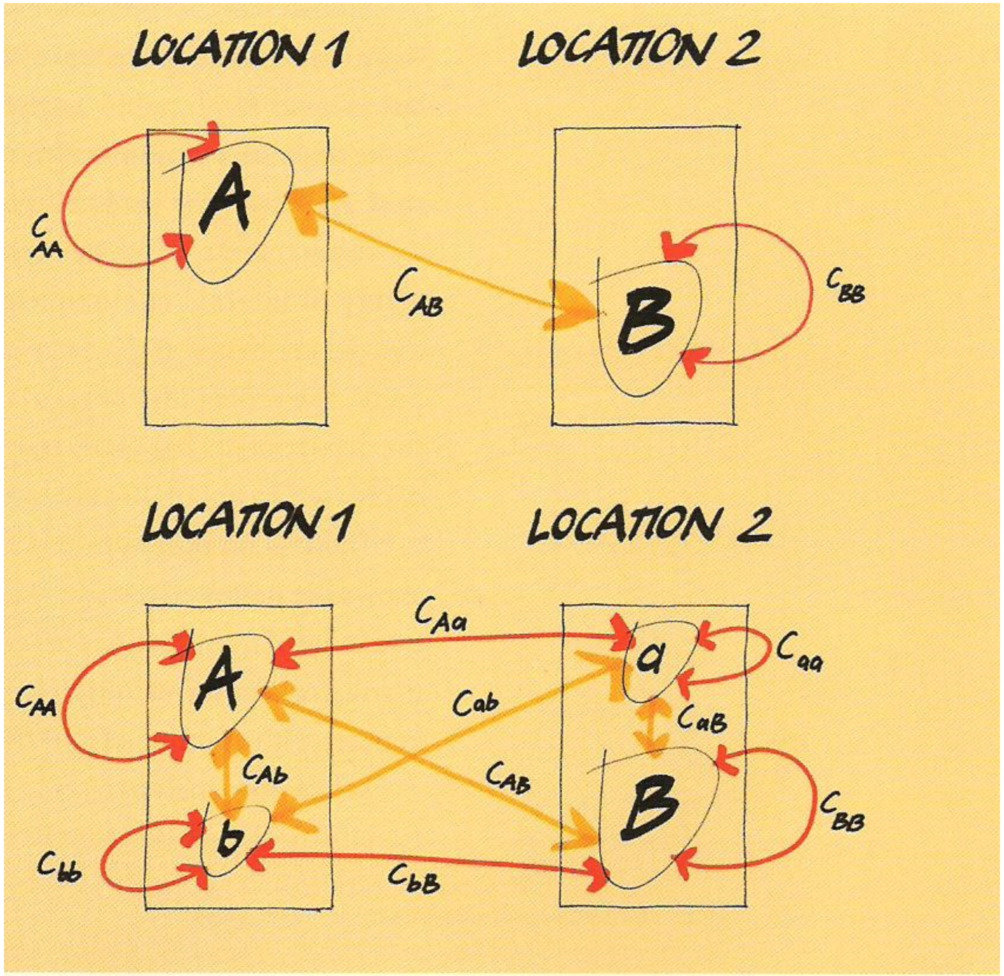
Communication across disciplines





Allen & Henn 2007

How about a "Mini-sabbatical" ?



Allen & Henn 2007

The challenges in interdisciplinary teams

commentary

Social engineering for virtual ‘big science’ in systems biology

Hiroaki Kitano, Samik Ghosh & Yukiko Matsuoka

A new type of big science is emerging that involves knowledge integration and collaboration among small sciences. Because open collaboration involves participants with diverse motivations and interests, social dynamics have a critical role in making the project successful. Thus, proper ‘social engineering’ will have greater role in scientific project planning and management in the future.

Learning from Ecology

Available online at www.sciencedirect.com

ScienceDirect

ELSEVIER

Current Opinion in Biotechnology

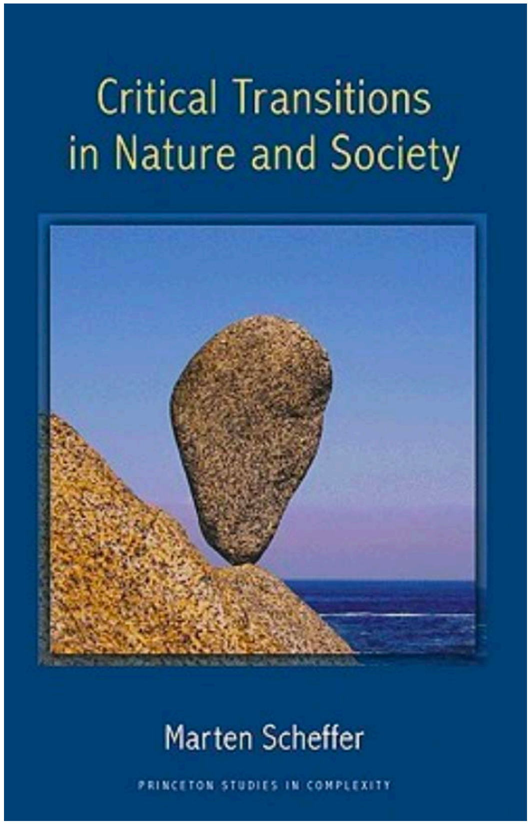
CrossMark

Critical transitions in chronic disease: transferring concepts from ecology to systems medicine

Christophe Trefois[1], Paul MA Antony[1], Jorge Goncalves[2], Alexander Skupin[3,4] and Rudi Balling[1]

Curr. Opin.Biotechn. 2015 Aug;34:48-55. doi: 10.1016/j.copbio.2014.11.020. Epub 2014 Dec 10.

Can we identify early warning signals for disease transitions?



Vol 461|3 September 2009|doi:10.1038/nature08227 nature

REVIEWS

Early-warning signals for critical transitions

Marten Scheffer[1], Jordi Bascompte[2], William A. Brock[3], Victor Brovkin[5], Stephen R. Carpenter[4], Vasilis Dakos[1], Hermann Held[6], Egbert H. van Nes[1], Max Rietkerk[7] & George Sugihara[8]

Complex dynamical systems, ranging from ecosystems to financial markets and the climate, can have tipping points at which a sudden shift to a contrasting dynamical regime may occur. Although predicting such critical points before they are reached is extremely difficult, work in different scientific fields is now suggesting the existence of generic early-warning signals that may indicate for a wide class of systems if a critical threshold is approaching.

COMPLEX SYSTEMS

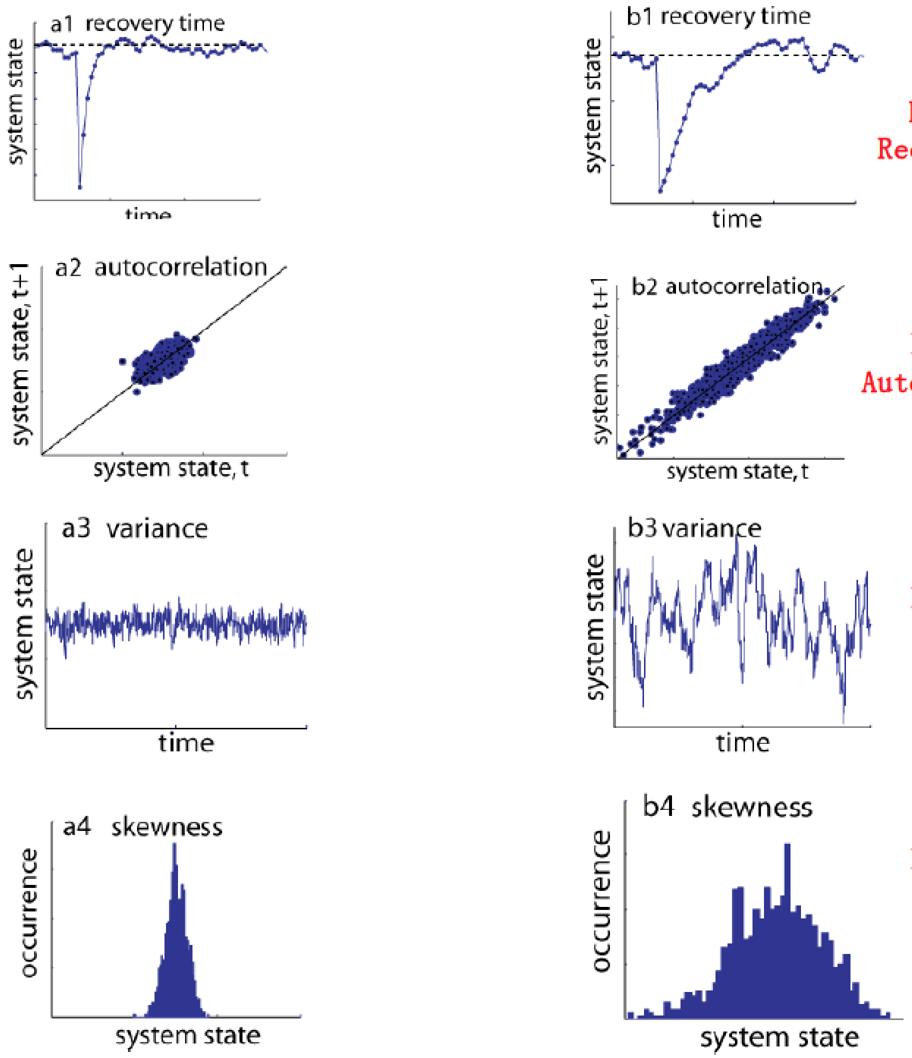
Foreseeing tipping points

Theory suggests that the risk of critical transitions in complex systems can be revealed by generic indicators. A lab study of extinction in plankton populations provides experimental support for that principle. SEE LETTER P. 456

MARTEN SCHEFFER

of a tipping point are based on the idea that,

Early warning signals



Decreased Recovery rate

Increased Autocorrelation

Increased Variance

Increased Skewness

The next generation of biomarkers

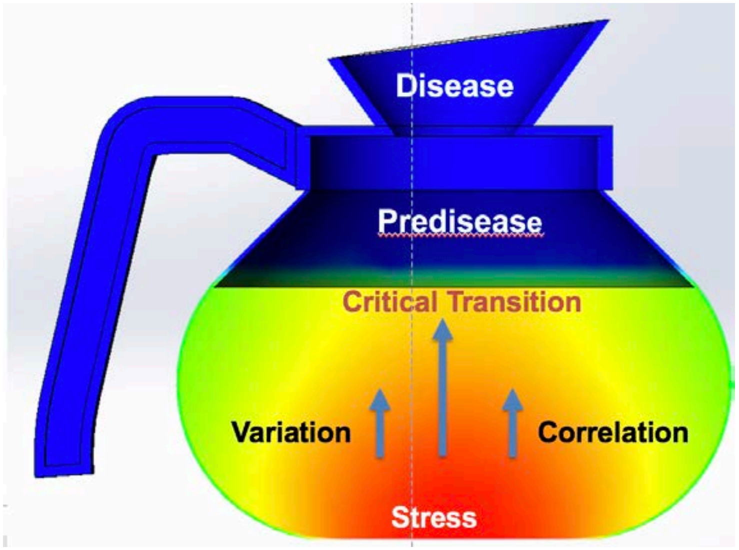
- More than mean and variance -

COMMENTARY PNAS | November 26, 2013 | vol. 110 | no. 48 | 19181–19182

Thermodynamically inspired classifier for molecular phenotypes of health and disease

Marc T. Facciotti[1]
Department of Biomedical Engineering and Genome Center, University of California, Davis, CA 95616

irrespective of their abundance and thus potential influence on cellular state.



Critical transitions in cell differentiation

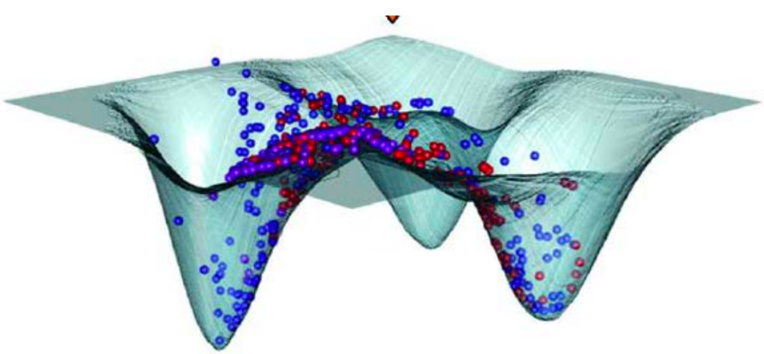
RESEARCH ARTICLE

Cell Fate Decision as High-Dimensional Critical State Transition

Mitra Mojtahedi[1,2☯], Alexander Skupin[2,3☯], Joseph Zhou[2], Ivan G. Castaño[1,4], Rebecca Y. Y. Leong-Quong[1], Hannah Chang[5], Kalliopi Trachana[2], Alessandro Giuliani[6], Sui Huang[1,2]*

Epo **Il3/GM-CSF**

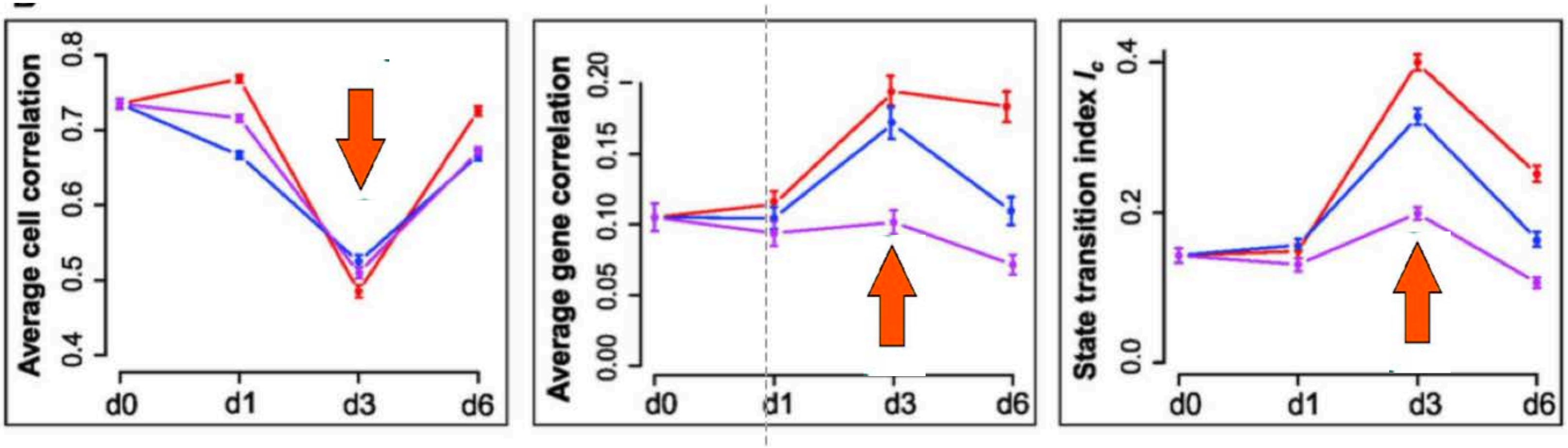
Erythroid **Myeloid**



PLoS Biol 14(12), 2016

Critical transitions in cell differentiation

Cell correlation | Gene correlation | Ratio (I_c)



$$I_C(t) = \frac{\langle |R(g_i, g_j)| \rangle}{\langle R(S^k, S^l) \rangle}$$

Mojtahedi et al. PLOS Biol. 2016

Dynamical network biomarkers

SCIENTIFIC REPORTS

OPEN

SUBJECT AREAS:
COMPUTATIONAL BIOLOGY
BIOINFORMATICS
BIOPHYSICS
CANCER MODELS

Detecting early-warning signals for sudden deterioration of complex diseases by dynamical network biomarkers

Luonan Chen[1,2], Rui Liu[2], Zhi-Ping Liu[1], Meiyi Li[1] & Kazuyuki Aihara[2]

(Chen et al., Scientific Reports 2012)

PLOS | COMPUTATIONAL BIOLOGY

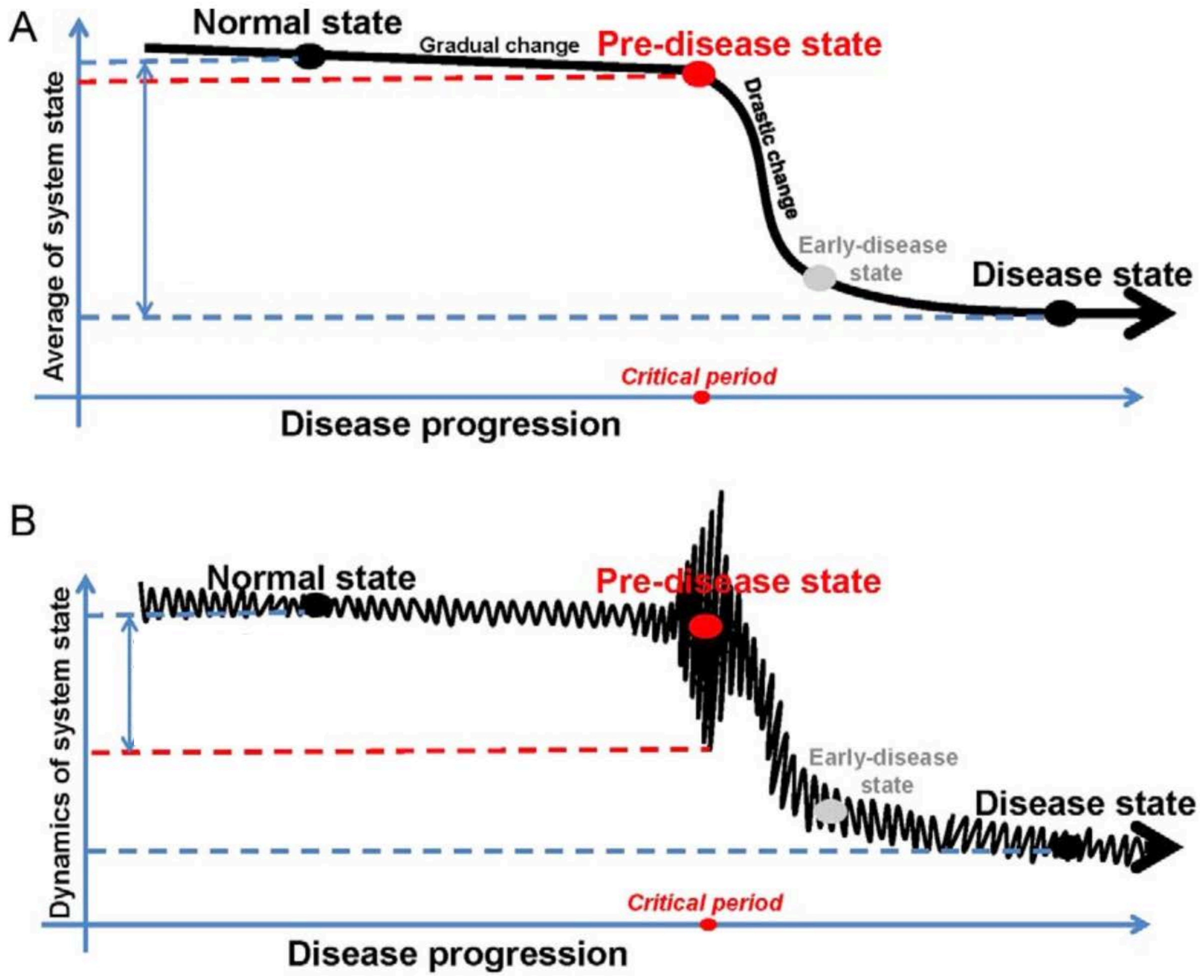
RESEARCH ARTICLE

Quantifying critical states of complex diseases using single-sample dynamic network biomarkers

Xiaoping Liu[1,2,3,4☯‡], Xiao Chang[1,2☯‡], Rui Liu[5], Xiangtian Yu[3], Luonan Chen[1,3,6*], Kazuyuki Aihara[1*]

1 Institute of Industrial Science, the University of Tokyo, Tokyo, Japan, **2** College of Statistics and Applied Mathematics, Anhui University of Finance and Economics, Bengbu, Anhui Province, China, **3** Key Laboratory of Systems Biology, CAS Center for Excellence in Molecular Cell Science, Innovation Center for Cell Signaling Network, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, China, **4** School of Mathematics and Statistics, Shandong University at Weihai, Weihai, China, **5** School of Mathematics, South China University of Technology, Guangzhou, China, **6** School of Life Science and Technology, ShanghaiTech University, Shanghai, China

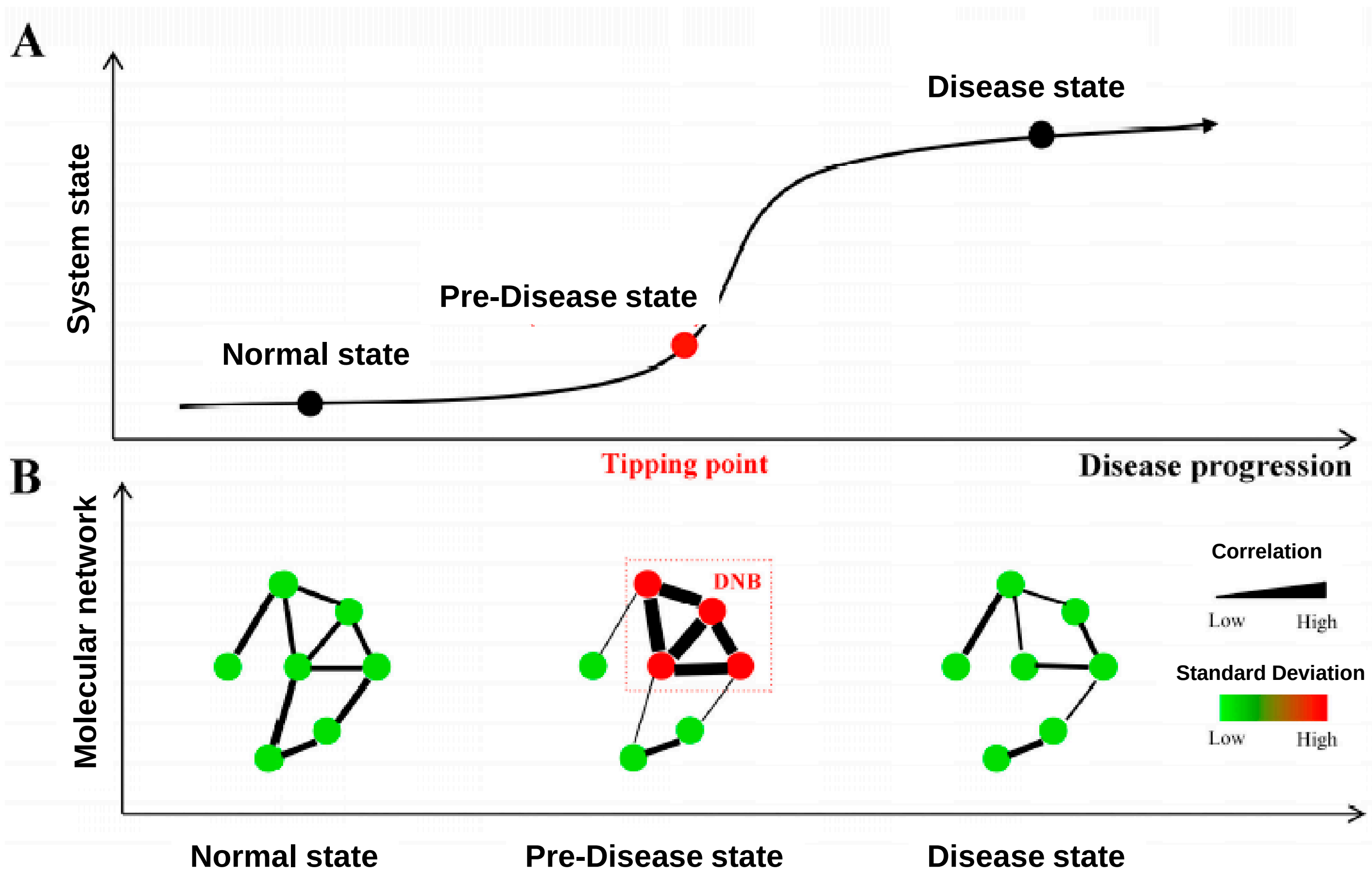
Dynamical Network Biomarkers as early warning signals



Liu, R. et al. 2013

Using Gene Variation and Correlation

as an early warning signal



Luonan Cheng et al.

Identifying critical transitions from EHR-data

PLOS | ONE

RESEARCH ARTICLE

Defining and characterizing the critical transition state prior to the type 2 diabetes disease

Bo Jin[1☯], Rui Liu[2,3☯], Shiying Hao[2,4☯], Zhen Li[2,5☯], Chunqing Zhu[1], Xin Zhou[6], Pei Chen[7], Tianyun Fu[1], Zhongkai Hu[2], Qian Wu[8], Wei Liu[8], Daowei Liu[8], Yunxian Yu[9], Yan Zhang[2,10], Doff B. McElhinney[2,4], Yu-Ming Li[6], Devore S Culver[11], Shaun T. Alfreds[11], Frank Stearns[1], Karl G. Sylvester[2], Eric Widen[1], Xuefeng B. Ling[2,4,12]*

Method

We applied the transition-based network entropy methodology which previously identified a dynamic driver network (DDN) underlying the critical T2DM transition at the tissue molecular biological level. To profile pre-disease phenotypical changes that indicated a critical transition state, a cohort of 7,334 patients was assembled from the Maine State Health Information Exchange (HIE). These patients all had their first confirmative diagnosis of T2DM between January 1, 2013 and June 30, 2013. The cohort's EMRs from the 24 months preceding their date of first T2DM diagnosis were extracted.

Results

Analysis of these patients' pre-disease clinical history identified a dynamic driver network (DDN) and an associated critical transition state six months prior to their first confirmative T2DM state.

Gene Variation and Correlation at transition points

Choose genes with high fluctuations → Functional analysis of DNB → Identification of DNB (by 3 conditions) → Cluster genes with high correlations

Deviation Test (Step 1)

Correlation Test (Step 2)

Significance Test (Step 3)

Functional Test (Step 4)

$$I_m = \frac{SD_{in} \cdot PCC_{in}}{PCC_{out}}$$

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Luonan Cheng et al.

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Can we use system-immanent ratio’s

to describe the state of a disease?

$$I_C(t) = \frac{\langle |R(g_i, g_j)| \rangle}{\langle R(S^k, S^l) \rangle},$$

Mojtahedi et al.

Immunometabolism as a potential switch-point in Parkinson`s disease

nature COMMUNICATIONS

ARTICLE

Received 13 Aug 2014 | Accepted 19 Feb 2015 | Published 26 Mar 2015

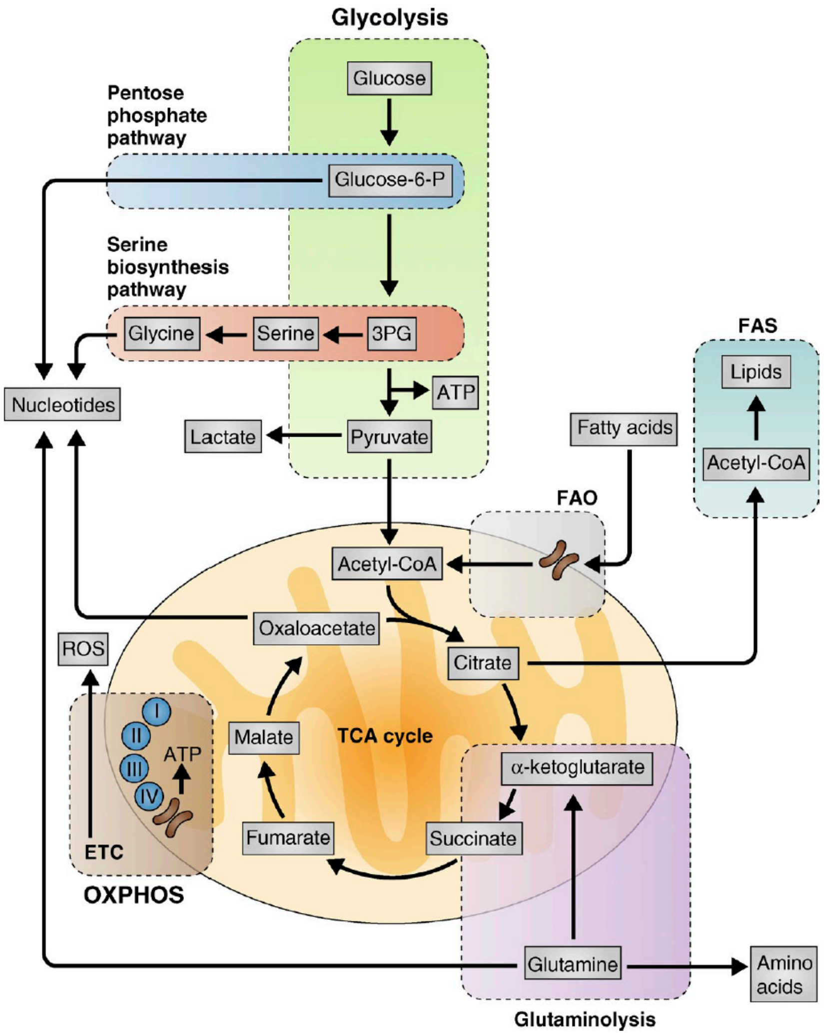
DOI: 10.1038/ncomms7692

OPEN

PD-1 alters T-cell metabolic reprogramming by inhibiting glycolysis and promoting lipolysis and fatty acid oxidation

Nikolaos Patsoukis[1,2,3], Kankana Bardhan[1,2,3], Pranam Chatterjee[1,2,3], Duygu Sari[1,2,3], Bianling Liu[1,2,3], Lauren N. Bell[4], Edward D. Karoly[4], Gordon J. Freeman[5], Victoria Petkova[1,2,3], Pankaj Seth[2,3,6], Lequn Li[1,2,3] & Vassiliki A. Boussiotis[1,2,3]

Modules in Metabolism



JEM Review

T cell metabolism drives immunity

Michael D. Buck, David O'Sullivan, and Erika L. Pearce

Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO 63110

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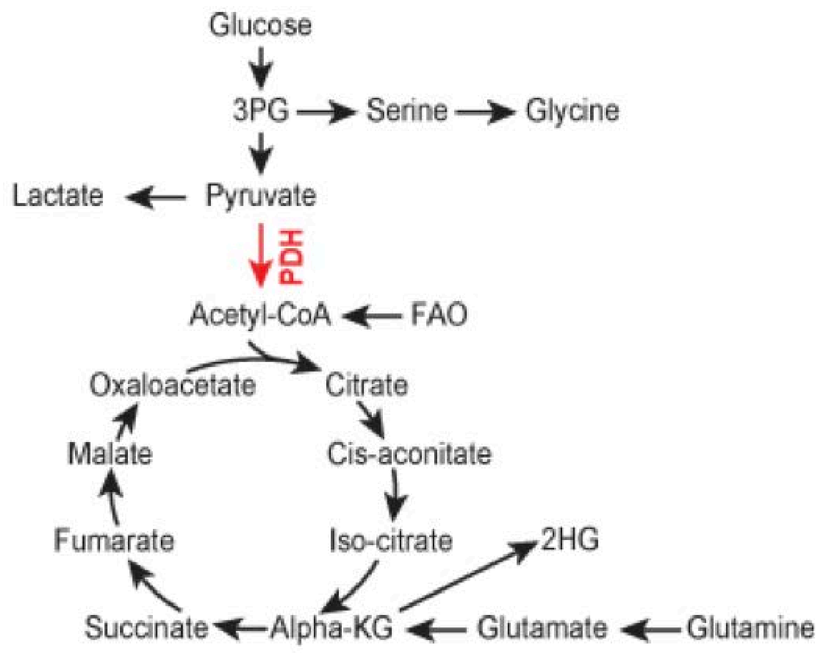
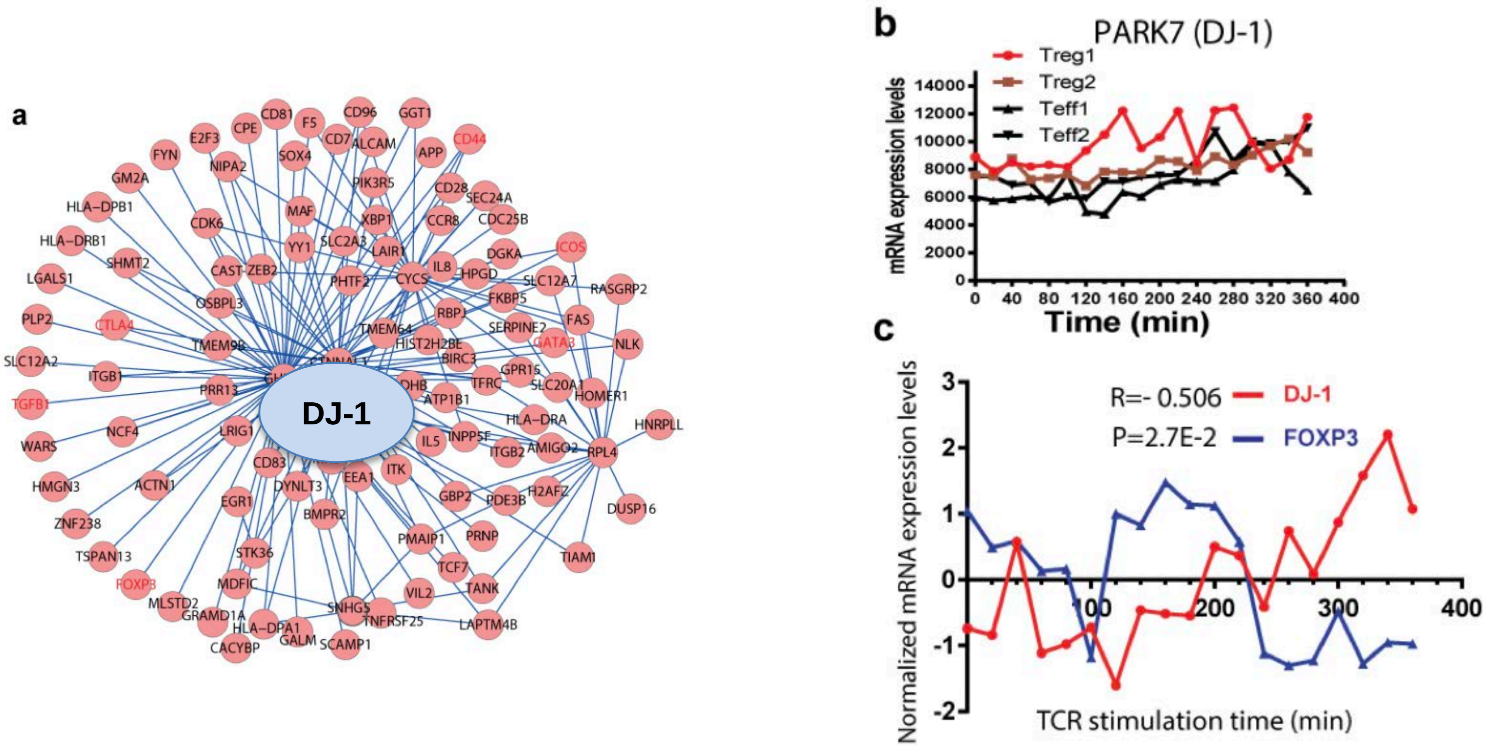
Can we identify meaningful ratio`s that provide information on robustness and fragility?



A central role of DJ-1/Park7 in energy metabolism



Egle Daniveluce, He Feng et al. (unpublished)

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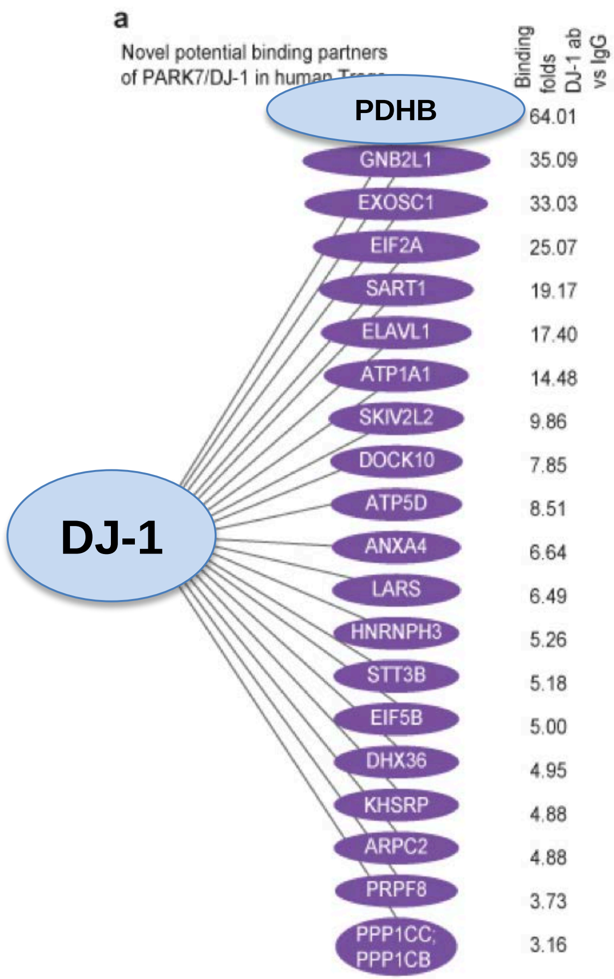
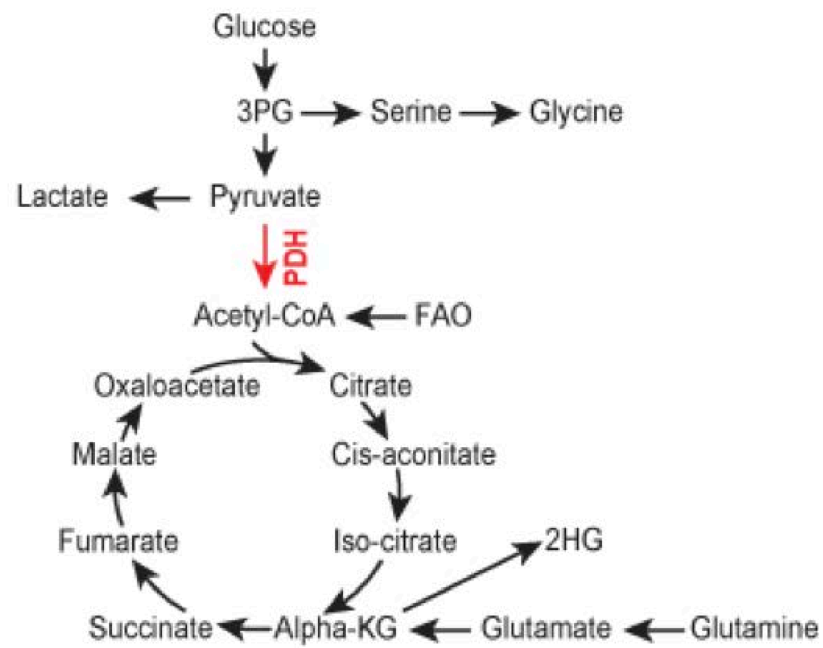
DJ-1 directly binds PHDB





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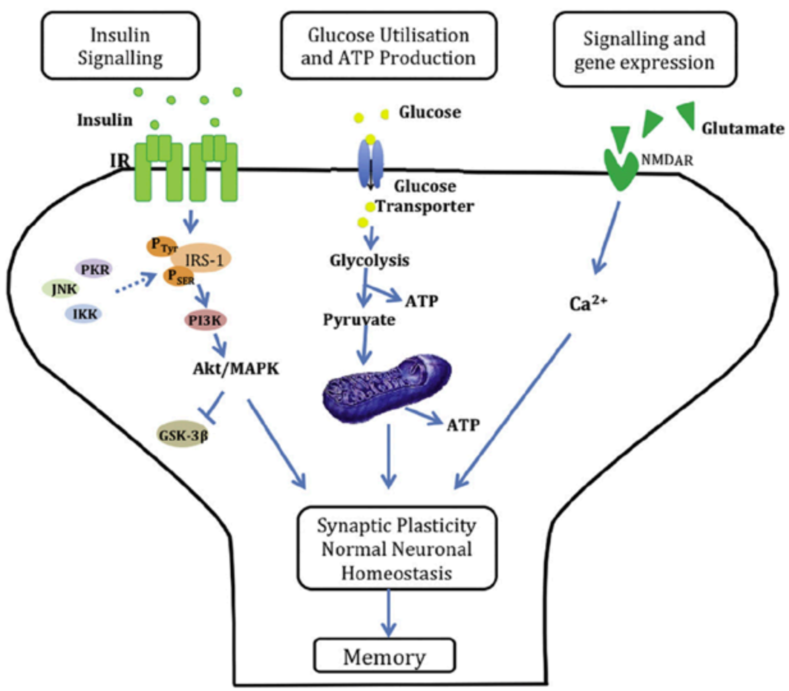
Insulin resistance, diabetes and neurodegeneration

G. Verdile et al. / Neurobiology of Disease 84 (2015) 22–38



Neurobiology of Disease 84 (2015) 22–38
Contents lists available at ScienceDirect
Neurobiology of Disease
journal homepage: www.elsevier.com/locate/ynbdi

Review

The role of type 2 diabetes in neurodegeneration

Giuseppe Verdile [a,b,c], Stephanie J. Fuller [c], Ralph N. Martins [a,b,c,*]

[a] School of Biomedical Sciences, CHIRI Biosciences, Curtin University, Bentley, Western Australia 6102, Australia
[b] Centre of Excellence for Alzheimer's Disease Research and Care, School of Medical Sciences, Edith Cowan University, Joondalup, Western Australia 6027, Australia
[c] Sir James McCusker Alzheimer's Disease Research Unit, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Crawley, Western Australia 6009, Australia

Is Parkinson disease the Diabetes of the brain?

Epidemiology/Health Services Research
ORIGINAL ARTICLE

Diabetes and the Risk of Developing Parkinson's Disease in Denmark

EVA SCHERNHAMMER, MD[1,2,3]
JOHNNI HANSEN, PHD[4]
KATHRINE RUGBJERG, PHD[4]
LENE WERMUTH, MD[5]
BEATE RITZ, MD[6]

OBJECTIVE—Insulin contributes to normal brain function. Previous studies have suggested associations between midlife diabetes and neurodegenerative diseases, including Parkinson's disease. Using Danish population registers, we investigated whether a history of diabetes or the use of antidiabetes drugs was associated with Parkinson's disease.

RESEARCH DESIGN AND METHODS—From the nationwide Danish Hospital Register hospital records, we identified 1,931 patients with a first-time diagnosis of Parkinson's disease between 2001 and 2006. We randomly selected 9,651 population control subjects from the Central Population Registry and density matched them by birth year and sex. Pharmacy records comprising all antidiabetes and anti-Parkinson drug prescriptions in Denmark were available. Odds ratios (ORs) were estimated by logistic regression models.

RESULTS—Having diabetes, as defined by one or more hospitalizations and/or outpatient visits for the condition, was associated with a 36% increased risk of developing Parkinson's disease (OR 1.36 [95% CI 1.08–1.71]). Similarly, diabetes defined by the use of any antidiabetes medications was associated with a 35% increased Parkinson's disease risk (1.35 [1.10–1.65]). When diabetes was defined as the use of oral antidiabetes medications, effect estimates were stronger in women (2.92 [1.34–6.36]), whereas when diabetes was defined as any antidiabetes drug prescription, patients with early-onset Parkinson's disease were at highest risk (i.e., Parkinson's disease diagnosed before the age of 60 years; 3.07 [1.65–5.70]).

normal brain function, and insulin resistance may lead to neurodegenerative disease, as suggested by a large study (3) that reported a higher incidence of Alzheimer's disease in men who developed diabetes in midlife, particularly those without the apolipoprotein Eε4 allele known to increase the risk of Alzheimer's disease.

A number of previous observational studies (2,4–16) have evaluated the association between diabetes and Parkinson's disease and provided mixed results ranging from protective to no or positive associations. The aim of this specific analysis was to examine whether a history of diabetes and, as such, insulin resistance is linked to Parkinson's disease. Adding to previous literature, ours is the first and largest study to examine whether the type of treatment with antidiabetes drugs differentially affects the risk of developing Parkinson's disease. Our investigation was based on a large population-based

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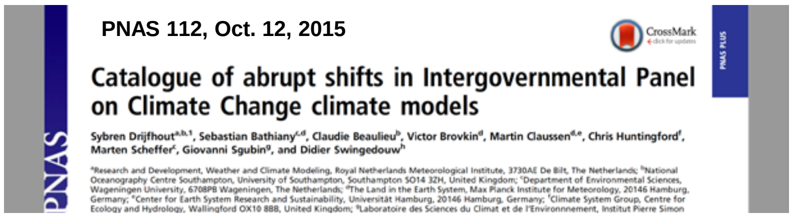
We need to systematically identify and classify critical transitions in disease pathogenesis

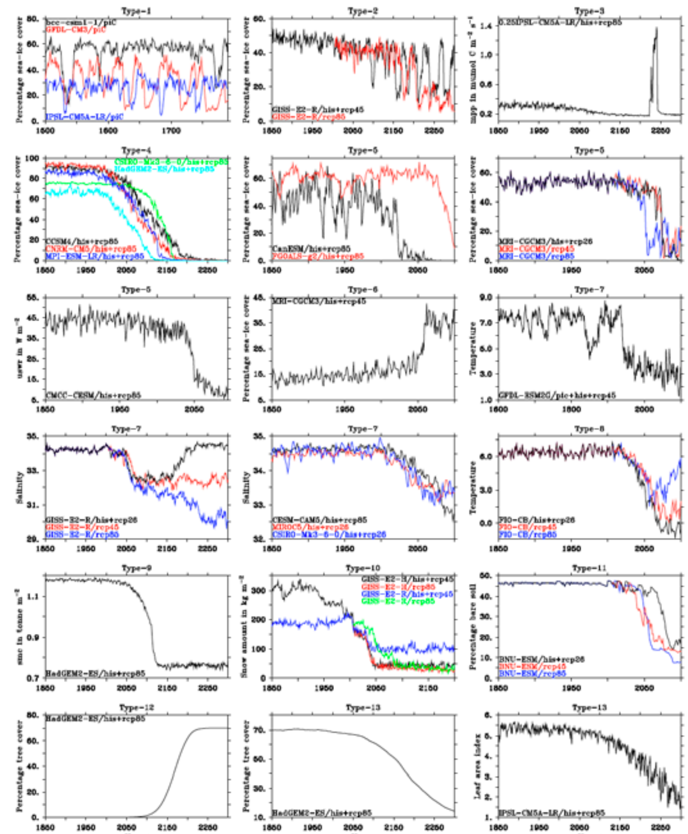
PNAS 112, Oct. 12, 2015


PNAS
PNAS PLUS

Catalogue of abrupt shifts in Intergovernmental Panel on Climate Change climate models

Sybren Drijfhout[a,b,1], Sebastian Bathiany[c,d], Claudie Beaulieu[b], Victor Brovkin[d], Martin Claussen[d,e], Chris Huntingford[f], Marten Scheffer[c], Giovanni Sgubin[g], and Didier Swingedouw[h]

[a]Research and Development, Weather and Climate Modeling, Royal Netherlands Meteorological Institute, 3730AE De Bilt, The Netherlands; [b]National Oceanography Centre Southampton, University of Southampton, Southampton SO14 3ZH, United Kingdom; [c]Department of Environmental Sciences, Wageningen University, 6708PB Wageningen, The Netherlands; [d]The Land in the Earth System, Max Planck Institute for Meteorology, 20146 Hamburg, Germany; [e]Center for Earth System Research and Sustainability, Universität Hamburg, 20146 Hamburg, Germany; [f]Climate System Group, Centre for Ecology and Hydrology, Wallingford OX10 8BB, United Kingdom; [g]Laboratoire des Sciences du Climat et de l'Environnnement, Institut Pierre Simon



1. Thresholds
2. Upper and lower bounds
3. Slopes
4. Types of transitions
5. Underlying mechanisms

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Physics meets Biology

QB
Quantitative Biology 2013, 1(1): 50–53
DOI 10.1007/s40484-013-0002-6

PERSPECTIVE

Stochastic physics, complex systems and biology§

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Physics meets Biology

nature

14 January 1999 Volume 397 Issue no 6715

Can physics deliver another biological revolution?

Cultural, institutional, conceptual and linguistic barriers are being overcome as physicists and biologists recognize the scientific stimulus they can gain from each other. The United States is showing the way.

Control Theory:	Feedback, Optimisation, Games
Information Theory:	Entropy, Coding
Computational Complexity:	Decidability, P-NP
Dynamic Systems:	Stability, Bifurcation, Chaos
Statistical Physics:	Phase Transitions, Critical Phenomena

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