COGNITIVE NEUROSCIENCE

Ubiquity of criticality in neural function across scales: recent empirical findings, speculations an caveats

Date:
Wednesday, 11 April, 2018 - 14:30

Seminars

Prof. Dante Chialvo (Center for Complex Systems & Brain Sciences -CEMSC3 - UNSAM - Buenos Aires, Argentina)

THEORETICAL PARTICLE PHYSICS

Implications of Higgs Vacuum Metastability

Jose Espinosa

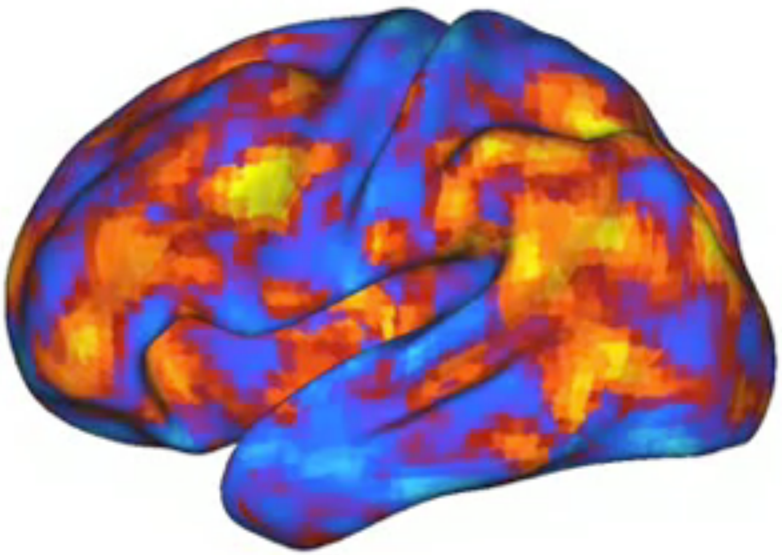
(IFAE Barcellona)

Room 005

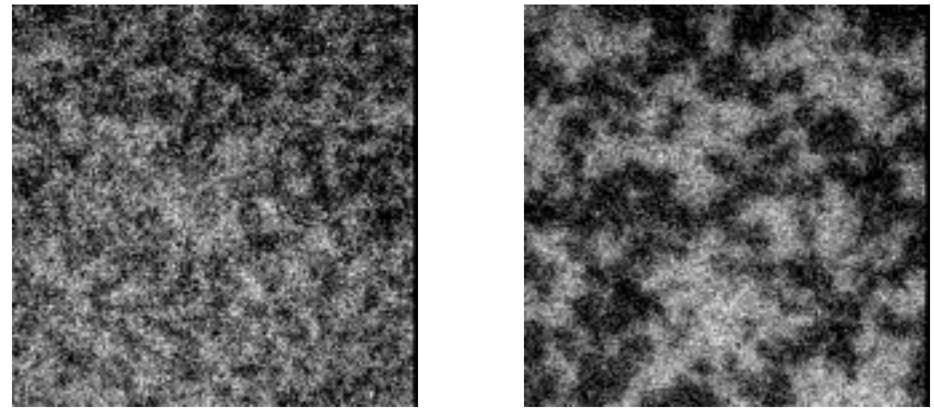
Wed, Apr 11 2018, 14:30

The Standard Model electroweak vacuum lies very close to the boundary between stability and metastability, with the last option being the most likely. I will discuss a) the interplay of this so-called "near-criticality" with physics beyond the Standard Model including possible Planckian effects; b) the main challenges that the survival of the electroweak vacuum faces during the evolution of the Universe, and c) possible signatures of this instability showing how Higgs fluctuations during inflation might provide dark matter in the form of primordial black holes as well as a background of potentially observable gravitational waves.

Life at the edge: complexity and criticality in biological function

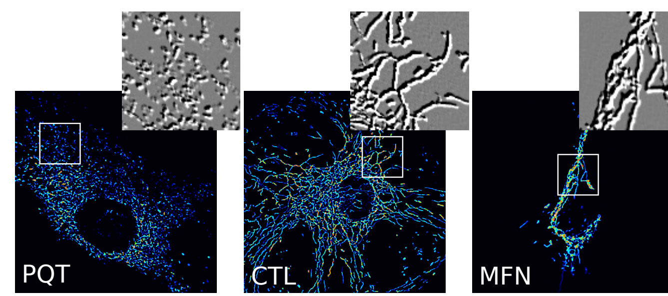


brain



lipid bilayer

protein



mitochondria

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"The laws of physics are simple but nature is complex".

CONICET
Cemsc³
Centro de Estudios Multidisciplinarios en Sistemas Complejos y Ciencias del Cerebro
UNSAM UNIVERSIDAD NACIONAL DE SAN MARTÍN
ESCUELA DE CIENCIA Y TECNOLOGÍA

Outline

Today -Why life is always found near criticality? (a 10 minutes manifesto for the non-cognoscenti on “Not too rigid, neither very flexible”)

-We apply these ideas to:

Today
- Brains (results on critical brain dynamics)
- Proteins (finite size scaling analysis on NMR data from the PDB database) 15 min. (with Y.T. Tang,Physical Review Letters 118, 088102, 2017)
- Mitochondria (critical fusion-fision balance of the mitochondrial network) 15 min. (with N&E Zamponi et al, Nature Sci. Reports 8, 363, 2018)

-Summary & questions

"In god we trust. All others, bring data" (W. Edwards Deming)

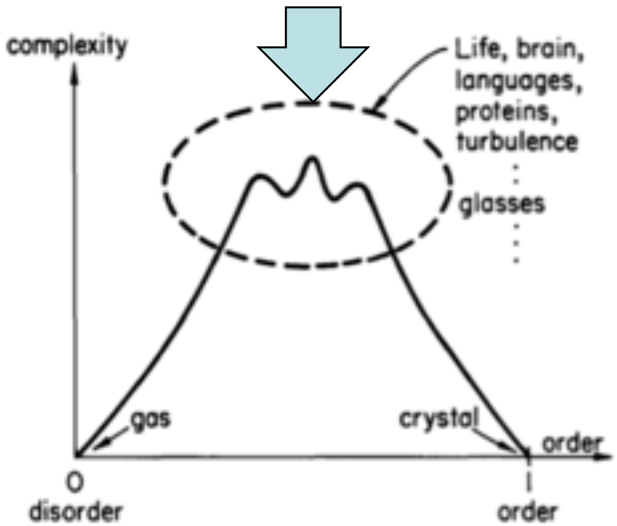
- *"Emergent complex neural dynamics"* Chialvo DR, Nature Physics 6 (10), 744-750 (2010)
- *"Learning from mistakes"* DR Chialvo, P Bak. Neuroscience 90 (4), 1137-1148 (1997).
- *"What kind of noise is brain noise?"* Fraiman & Chialvo, Frontiers in Phys., (2011).
- *"Criticality in large-scale brain fMRI dynamics…"* Frontiers in Phys. (2012).
- "*Brain organization into resting state networks emerges from the connectome at criticality"* Haimovici et al., Physical Review Letters, 110 (17), 178101 (2013).
- *"Large-scale signatures of unconsciousness are consistent with a departure from critical dynamics".* Journal of The Royal Society Interface, 13 (114), 20151027 (2016).
- *"Critical Fluctuations in the Native State of Proteins"* Tang QY et al., Physical Review Letters 118 (8), 088102 (2017).
- "*Mitochondrial network complexity emerges from fission/fusion dynamics"* Zamponi N, et al. Scientific Reports 8 (1), 363 (2018).
- "*La mente es crítica"* J. Marro & D. Chialvo. Univ. of Granada Editora, (2017).

*The results we describe are not anecdotal, they were already generalized to other systems, scales and setups by a number of authors.

80's

Intuition

critical



H. Frauenfelder NYAS 1987

90's

Theory

Including Self-Organized Criticality

K. Christensen, D. Chialvo, Per Bak & Z.Olami. Brookhaven National Lab. (Feb. 1992).

nowadays

Experiments

Physicals, social and biological systems are shown to be complex because the operate near criticality.

"A Fundamental Theory to Model the Mind" by Jennifer Ouellette in Quanta Magazine and Scientific American April, 2014.

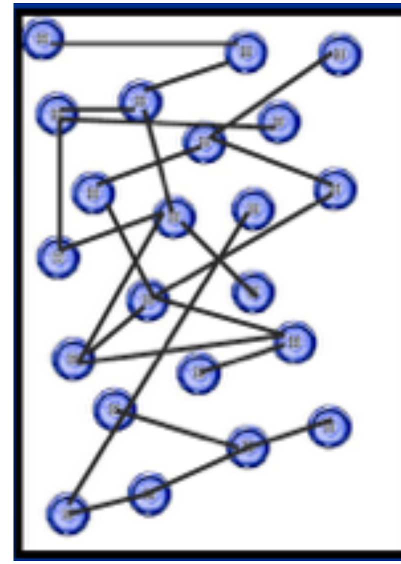
"Criticality and phase transitions in biology" by Philip Ball in New Scientist, 2014.

"La mente es crítica" by J. Marro & D. Chialvo. Granada Editora, 2017

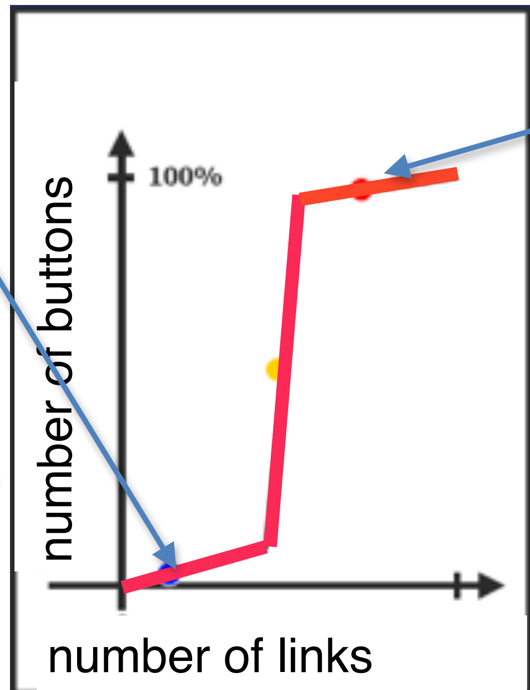
What means to be “Critical” Example 1: buttons

disconnected phase

continuos phase transition

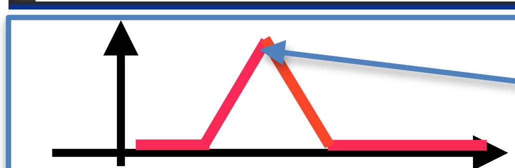


connected phase



do it many times and plot the average and the variance of the number of buttons

S.D. of number of buttons



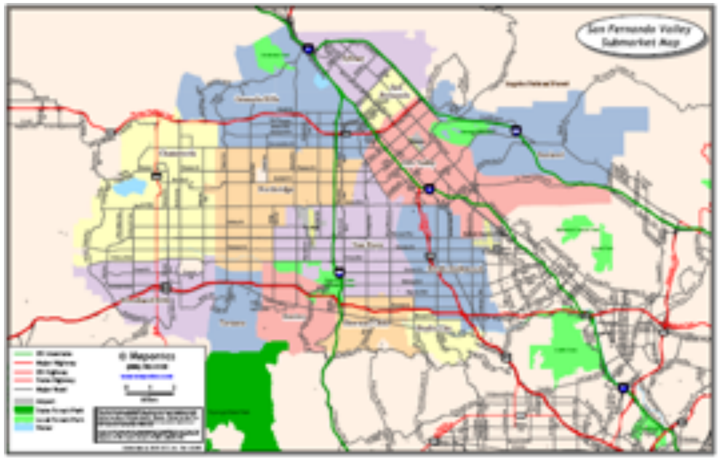
Moral: largest variability at the transition, largest cluster increases with N.

largest cluster ~ N^{∂}

peak variability ~ N^{β}

What means to be "Critical" (in 5 sec) Example 3: traffic

"solid"



+

=

"gas"

Structure
(the network of
streets)

+

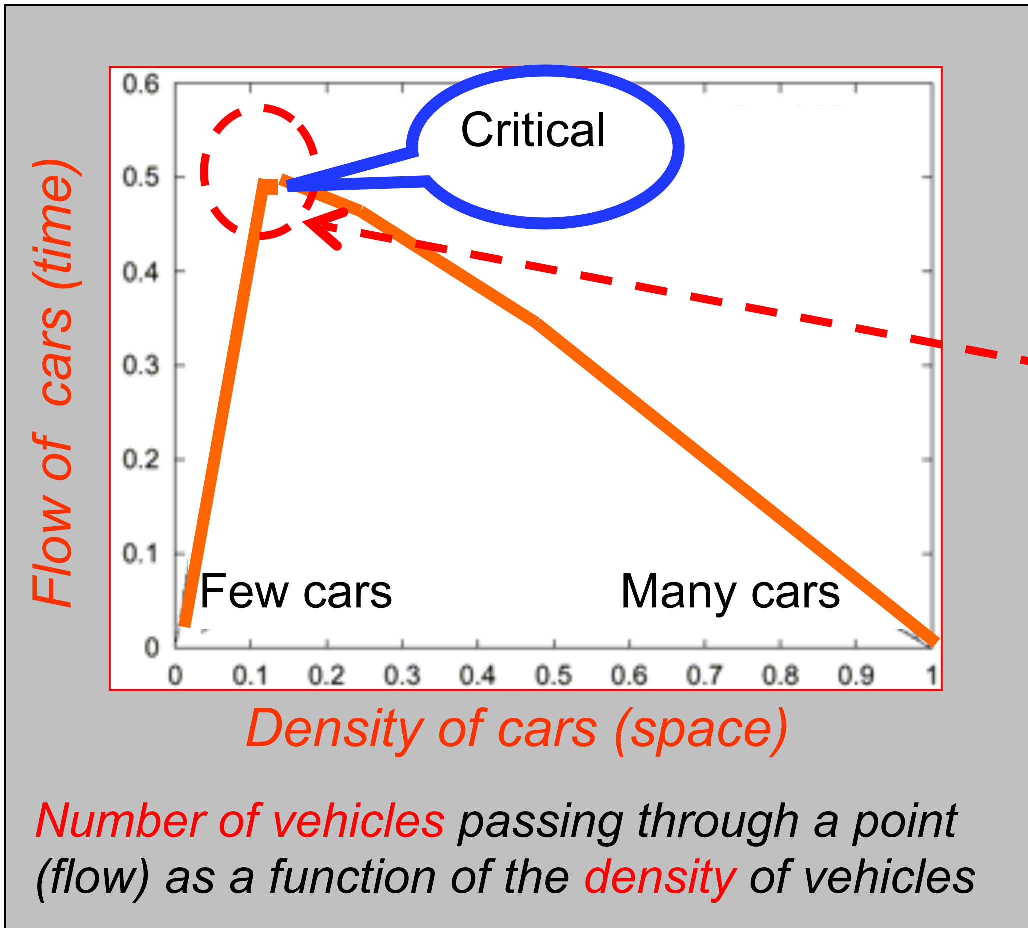
Individual
Non-linear
Dynamics
(drivers)

=

"phases"

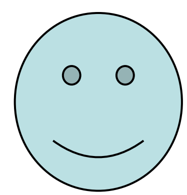
What means to be "Critical" -qualitatively speaking-

Traffic jams as a critical process

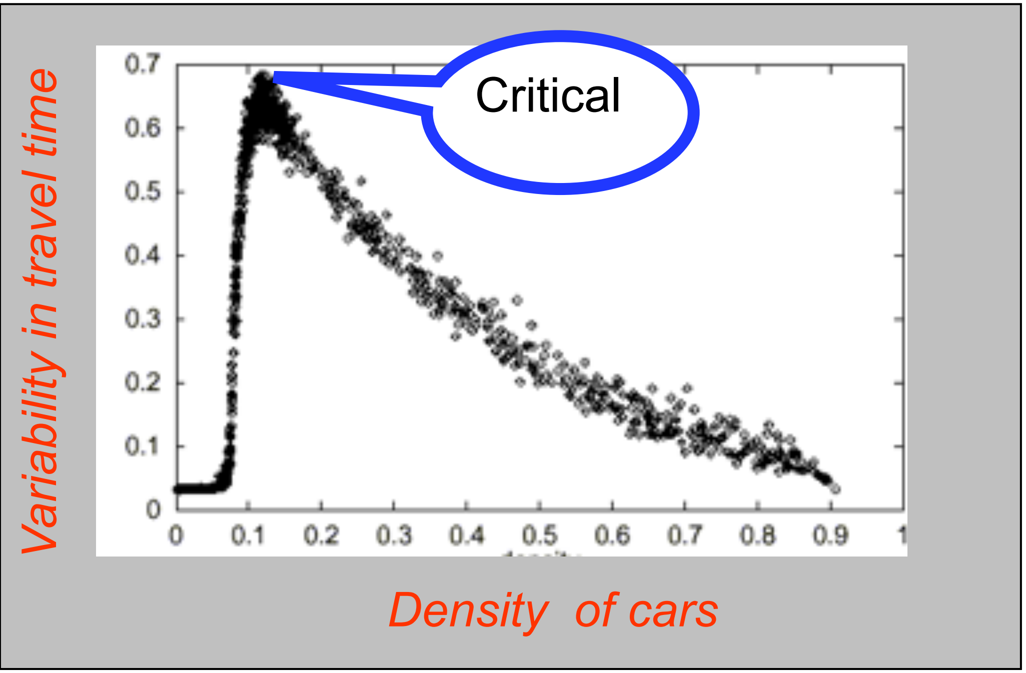


Number of vehicles passing through a point (flow) as a function of the density of vehicles

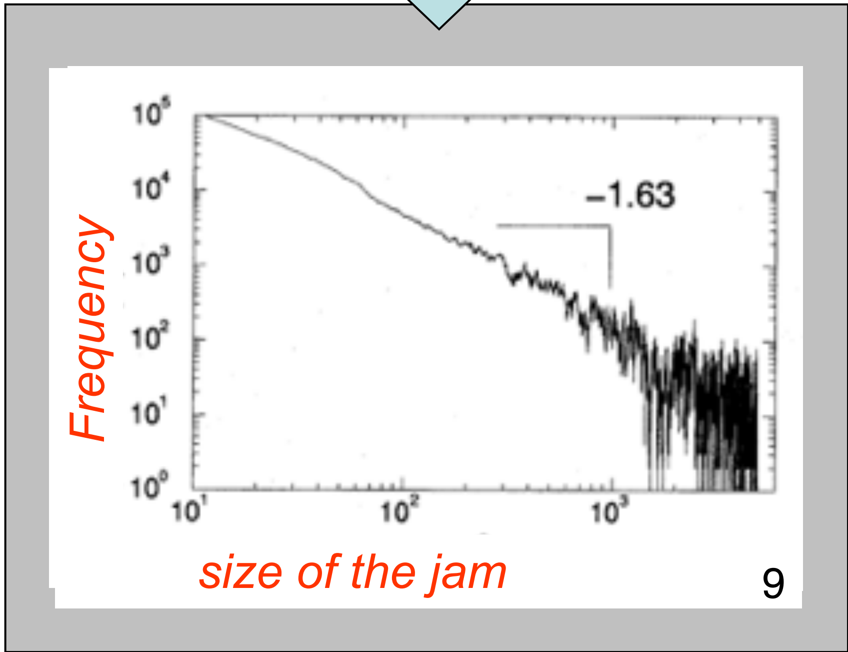
- *Two phases*
  - *- Free flow*
  - *-Jamming*
- *For the traffic engineer the maximum "efficiency" is at the Critical point*



- *For the driver the Critical density is the worst case!*



- *At criticality the travel time' variability is maximum*
- *Jams of all sizes*



- Higher efficiency and unpredictability both at criticality (counterintuitive, and important for management…)

Summing up, near criticality:

- The variability of the order parameter peaks at criticality (i.e, “susceptibility”) increasing with size as $N^{\text{some exponent}}$
- Clusters (jams/fires/buttons_bunch) of all sizes (i.e, long range spatial correlations observed as power law distributions of clusters).
- The action of a single driver/link/tree at any point in the system can have repercussion very far away both in time and space. (long range correlation and contingency)
- Despite that *interactions* are **short-range**, *correlations* can be **unlimited**, as large as the system itself.

These properties are *universal* (they don’t depend on the details of the system (cars, buttons, etc)

Second lecture

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-Summary & questions

If criticality is the solution …
what is the problem?

The brain can not work like a electrical circuit, because a circuit is something rigid (will need another brain to change the connections)

Synaptic interactions are fix (at the time scale of interest and very weak!!

Scale free clustering (ordering) without synchronization!

Second day

Remember: brain pairwise correlations are always weak

Strong ordering emerging of weak pairwise correlations

Vol 440|20 April 2006|doi:10.1038/nature04701 nature

ARTICLES

Weak pairwise correlations imply strongly correlated network states in a neural population

Elad Schneidman[1,2,3], Michael J. Berry II[2], Ronen Segev[2] & William Bialek[1,3]

Biological networks have so many possible states that exhaustive sampling is impossible. Successful analysis thus depends on simplifying hypotheses, but experiments on many systems hint that complicated, higher-order interactions among large groups of elements have an important role. Here we show, in the vertebrate retina, that weak correlations between pairs of neurons coexist with strongly collective behaviour in the responses of ten or more neurons. We find that this collective behaviour is described quantitatively by models that capture the observed pairwise correlations but assume no higher-order interactions. These maximum entropy models are equivalent to Ising models, and predict that larger networks are completely dominated by correlation effects. This suggests that the neural code has associative or error-correcting properties, and we provide preliminary evidence for such behaviour. As a first test for the generality of these ideas, we show that similar results are obtained from networks of cultured cortical neurons.

…The (yet) unsolved problem: how the brain manage to produce a huge range of cortical configurations in a flexible manner …

nature physics

REVIEW ARTICLE

PUBLISHED ONLINE: XX MONTH XXXX | DOI: 10.1038/NPHYS1803

Emergent complex neural dynamics

Dante R. Chialvo[1,2]★

A large repertoire of spatiotemporal activity patterns in the brain is the basis for adaptive behaviour. Understanding the mechanism by which the brain's hundred billion neurons and hundred trillion synapses manage to produce such a range of cortical configurations in a flexible manner remains a fundamental problem in neuroscience. One plausible solution is the involvement of universal mechanisms of emergent complex phenomena evident in dynamical systems poised near a critical point of a second-order phase transition. We review recent theoretical and empirical results supporting the notion that the brain is naturally poised near criticality, as well as its implications for better understanding of the brain.

History (2003-2005)

Scale-Free Brain Functional Networks

Victor M. Eguíluz,[1] Dante R. Chialvo,[2] Guillermo A. Cecchi,[3] Marwan Baliki,[2] and A. Vania Apkarian[2]
[1]*Instituto Mediterráneo de Estudios Avanzados, IMEDEA (CSIC-UIB), E07122 Palma de Mallorca, Spain*
[2]*Department of Physiology, Northwestern University, Chicago, Illinois, 60611, USA*
[3]*IBM T.J. Watson Research Center, 1101 Kitchawan Rd., Yorktown Heights, New York 10598, USA*
(Received 13 January 2004; published 6 January 2005)

Functional magnetic resonance imaging is used to extract *functional networks* connecting correlated human brain sites. Analysis of the resulting networks in different tasks shows that (a) the distribution of functional connections, and the probability of finding a link versus distance are both scale-free, (b) the characteristic path length is small and comparable with those of equivalent random networks, and (c) the clustering coefficient is orders of magnitude larger than those of equivalent random networks. All these properties, typical of scale-free small-world networks, reflect important functional information about brain states.

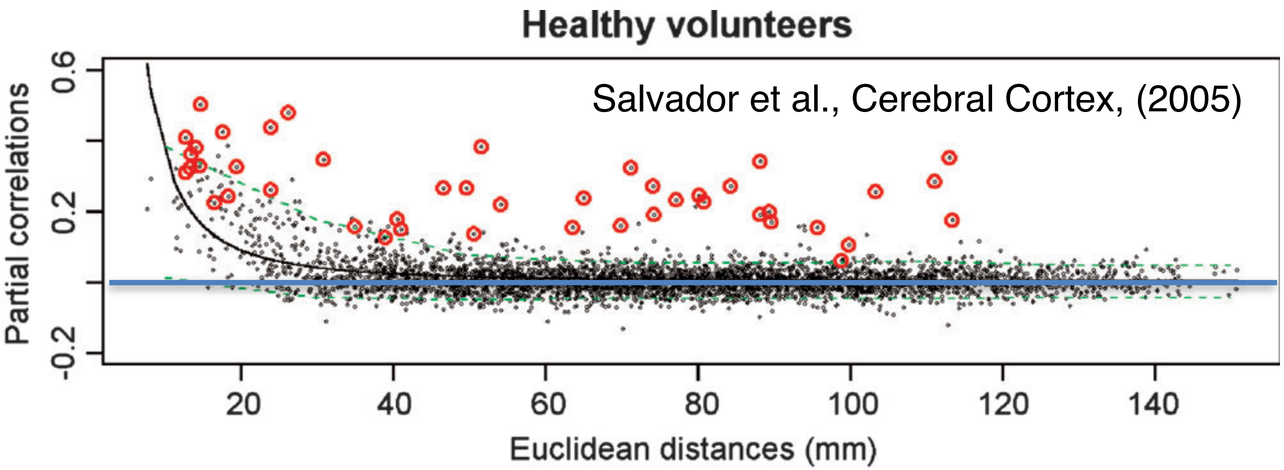
DOI: 10.1103/PhysRevLett.94.018102 PACS numbers: 87.18.Sn, 87.19.La, 89.75.Da, 89.75.Hc

ELSEVIER Review *TRENDS in Cognitive Sciences* Vol.8 No.9 September 2004 Full text provided by www.sciencedirect.com

Organization, development and function of complex brain networks

Olaf Sporns[1], Dante R. Chialvo[2], Marcus Kaiser[3] and Claus C. Hilgetag[3]

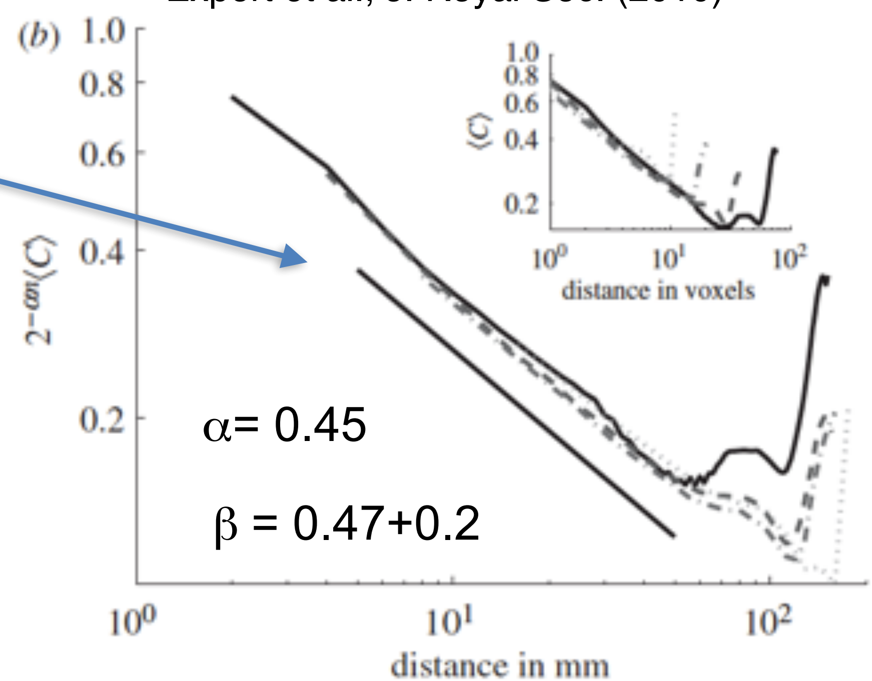
Brain mean two-point correlation function computed from Functional Magnetic Resonance Images during rest (no task)

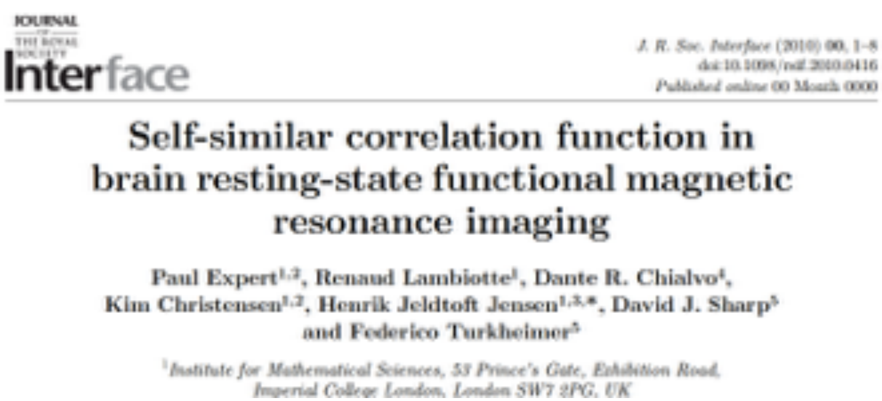


Most of C pairs are weak

Expert et al., J. Royal Soc. (2010)

C decays with distance as a power law





JOURNAL OF THE ROYAL SOCIETY Interface

J. R. Soc. Interface (2010) 00, 1–8
doi:10.1098/rsif.2010.0416
Published online 00 Month 0000

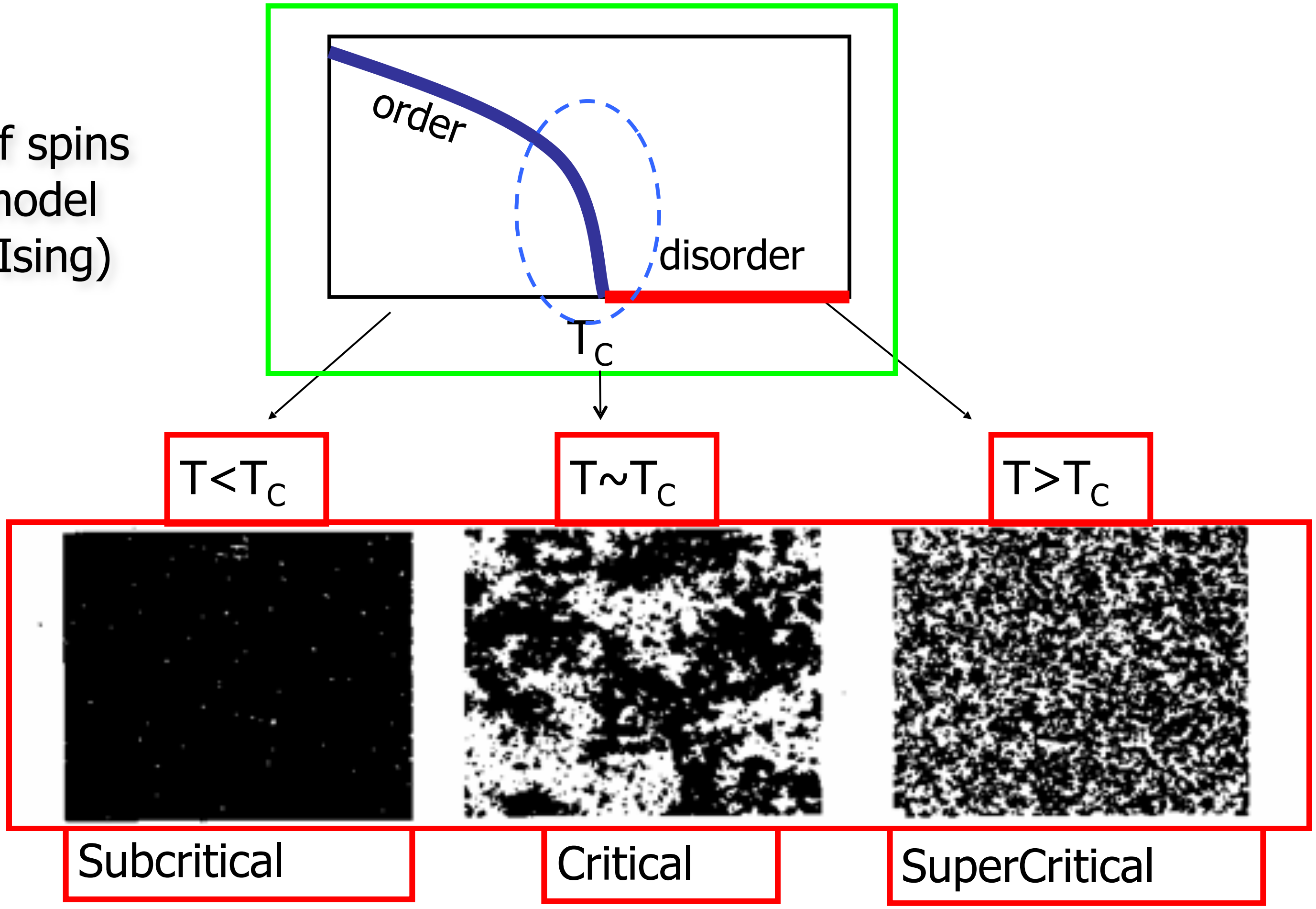
Self-similar correlation function in brain resting-state functional magnetic resonance imaging

Paul Expert[1,2], Renaud Lambiotte[1], Dante R. Chialvo[4], Kim Christensen[1,2], Henrik Jeldtoft Jensen[1,3,*], David J. Sharp[5] and Federico Turkheimer[5]

[1]Institute for Mathematical Sciences, 53 Prince's Gate, Exhibition Road, Imperial College London, London SW7 2PG, UK

Ferromagnetic-paramagnetic Phase-Transition

Snapshots of spins states in a model system (2D Ising)



Snapshots of spins states in the Ising model.

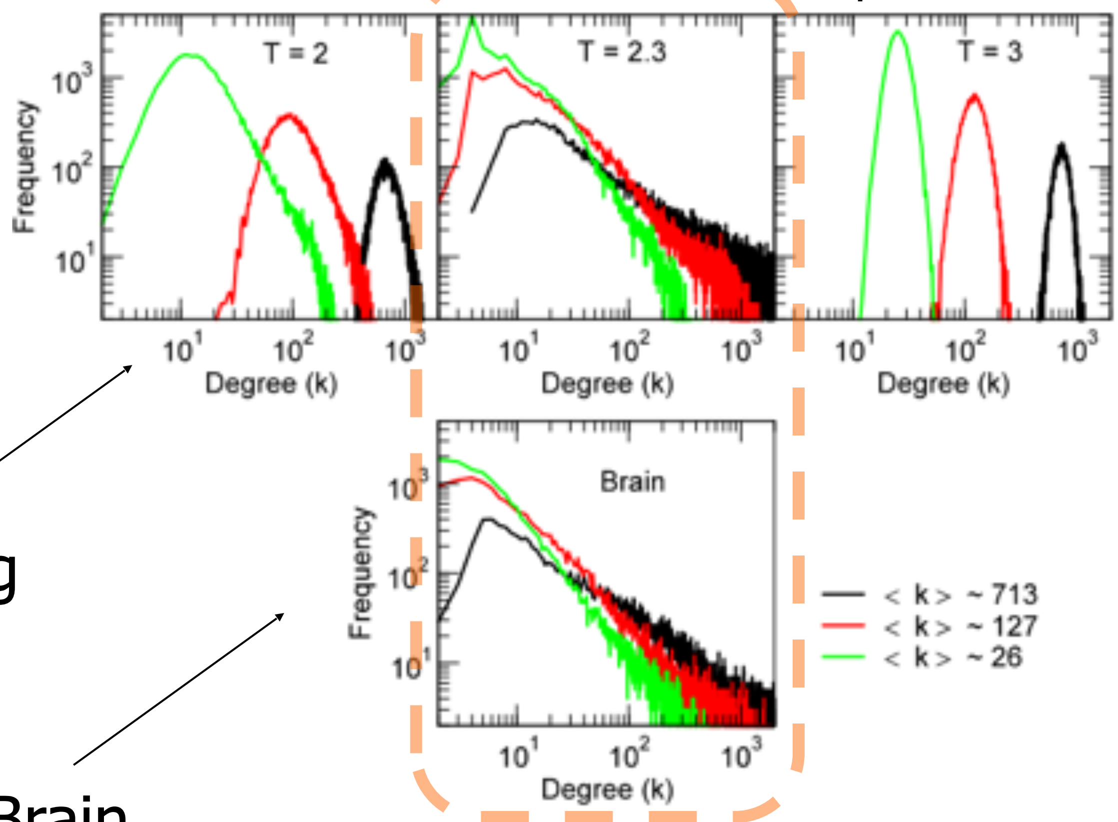
Long range correlations emerges at the phase transition

Despite its lattice (short range) interactions, Ising "funcional networks" (at criticality) mimic the fat tails of functional brain networks

SubCritical

Critical

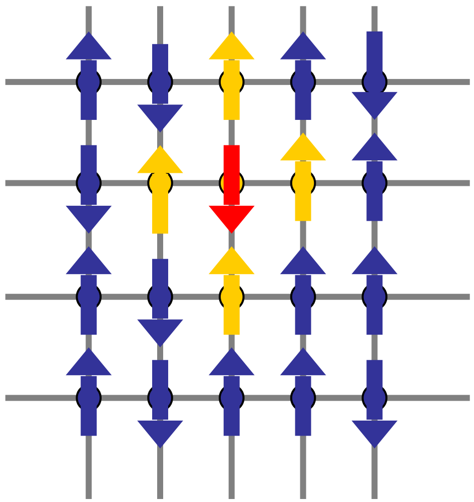
SuperCritical



Ising

Brain

Positive correlated networks



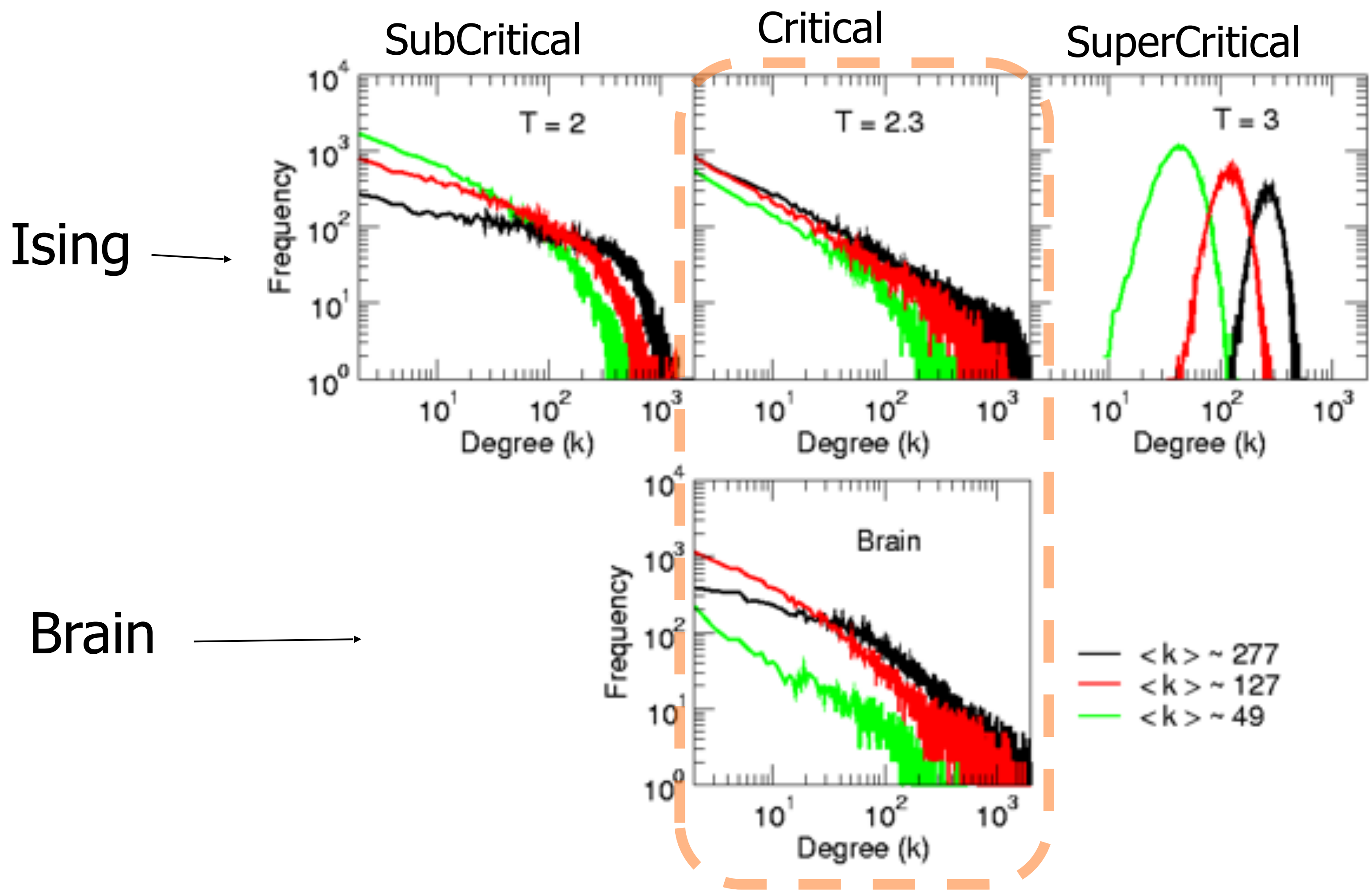
Only <u>local positive</u> interactions

$$\boxed{E=-J \sum_{<i,j>} S_i S_j - B \sum_k S_k}$$

From Chialvo, Balenzuela & Fraiman. The brain: What is critical about it? 2008 (arXiv.org/ cond-mat/0804.0032); Fraiman, Balenzuela, Foss & Chialvo, Ising like dynamics in large-scale brain networks. (arXiv.org/ cond-mat/0811.3721), Phys Rev. E. (2008).

Critical Ising networks mimic brain networks

Negative correlated networks



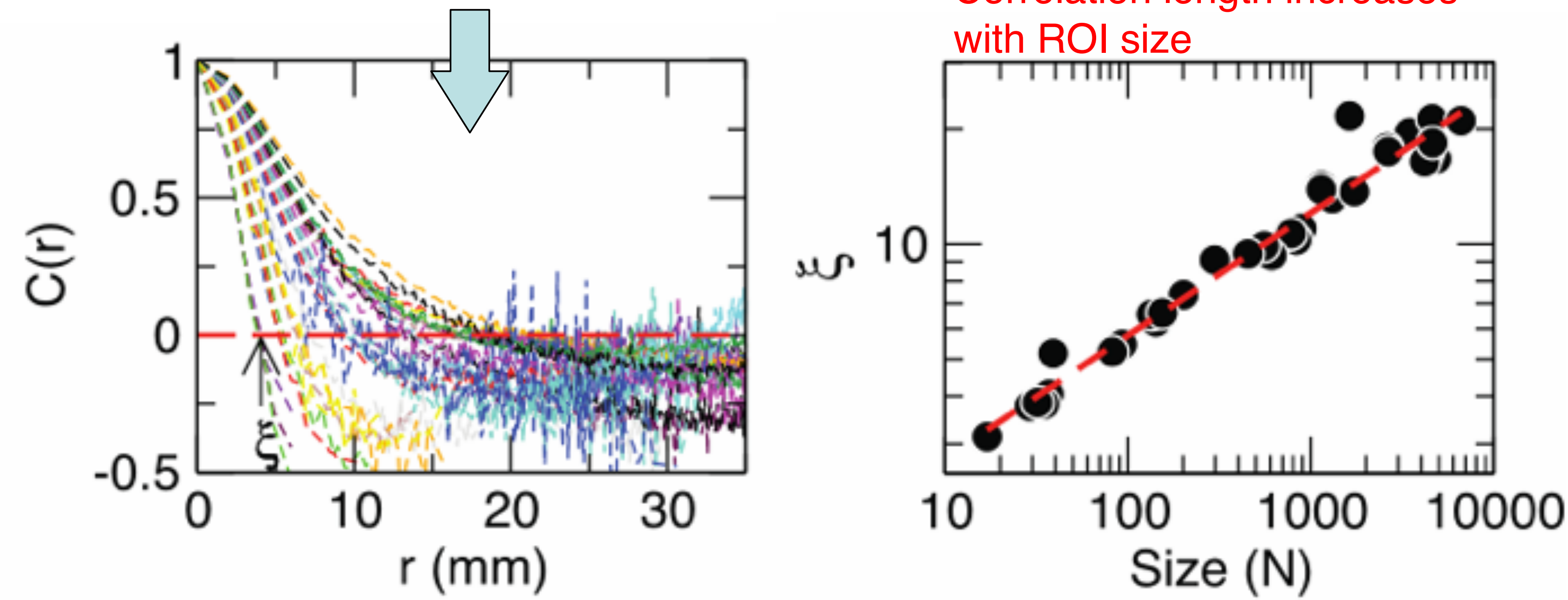
Negative correlations with fat tails similar to the brain data appear in the Ising data, despite the absence of negative "structural" interactions (i.e. no "inhibitory" connectivity).

We studied brain correlation functions …

What truly matters is the correlation length

Choose many ROIs.
Compute the average connected correlation function
for each ROI & plot it as a function of distance

Correlation length increases
with ROI size

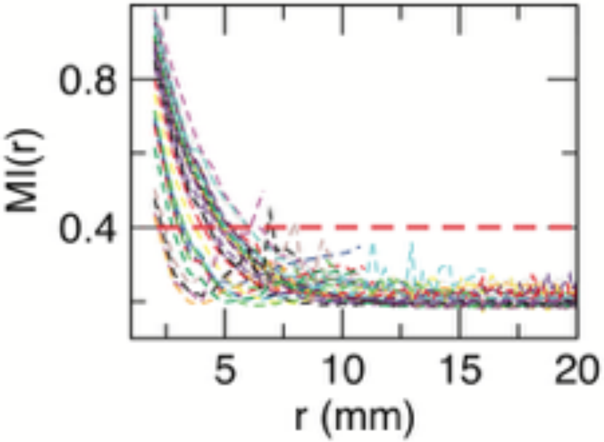


The bottom line: Big, intermediate and small ROI behaves all in the same way

For example: Two places 4 mm apart on a blob of 20 voxels are as correlated as those 40 mm apart on a blob of 4000 voxels

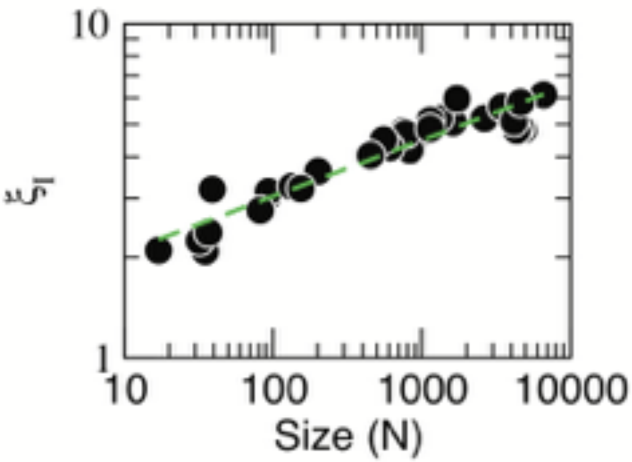
Chialvo DR & Fraiman D. (2010)

You could do the same for Mutual Information

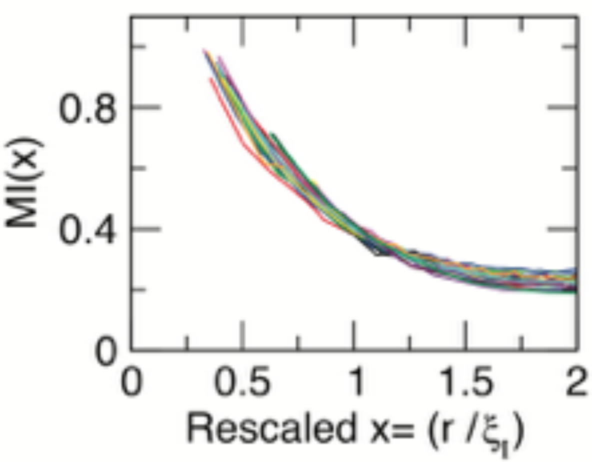


$$MI(X;Y) = H(X) - H(X \mid Y)$$

Mutual information MI(r) as a function of distance r averaged over all time series of each of the ROI.



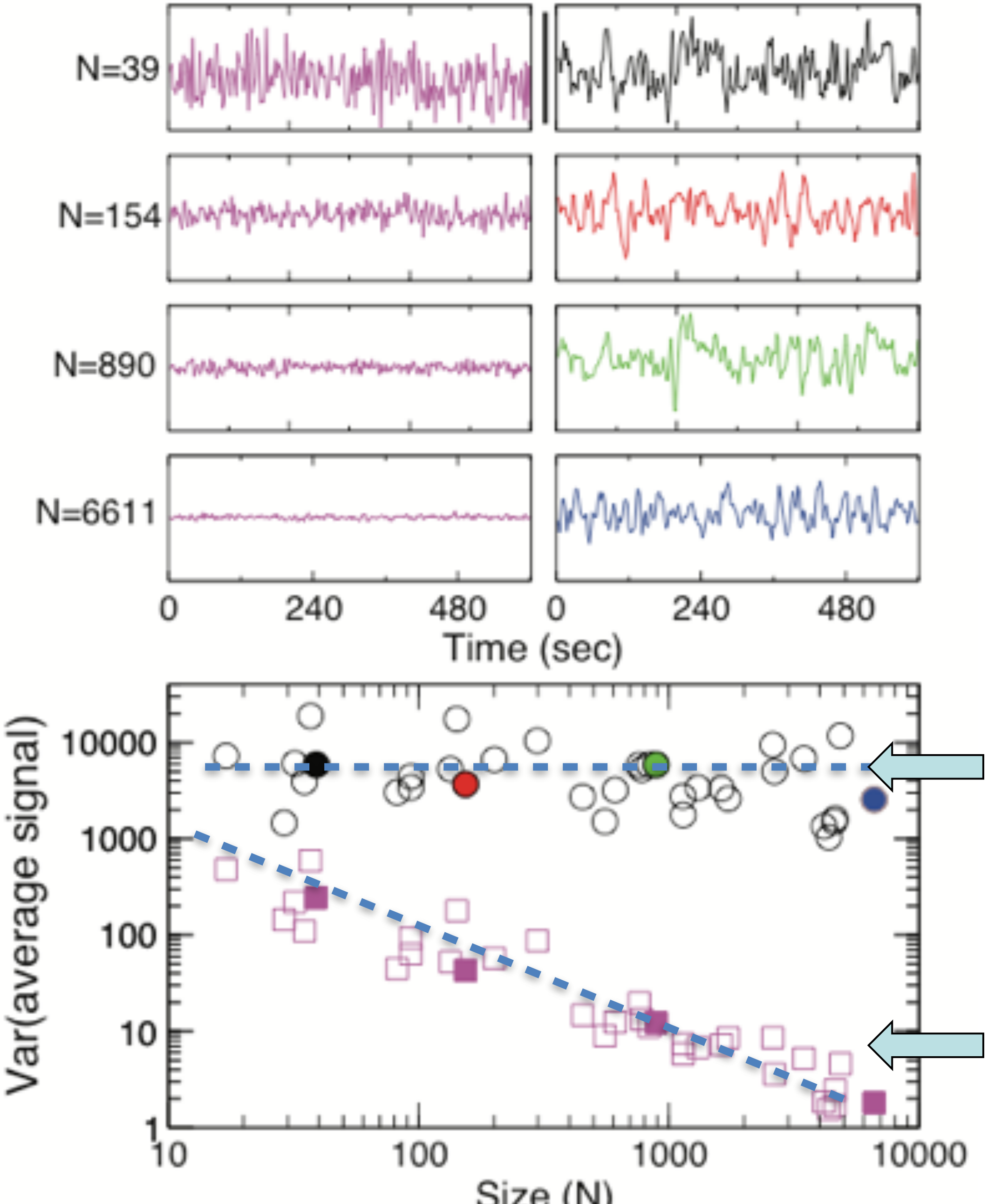
Mutual information increases with cluster size.



Rescaled mutual information

Chialvo DR & Fraiman D. (2010)

Consequences of the increase in Correlation Length:
Anomalous scaling of the variance



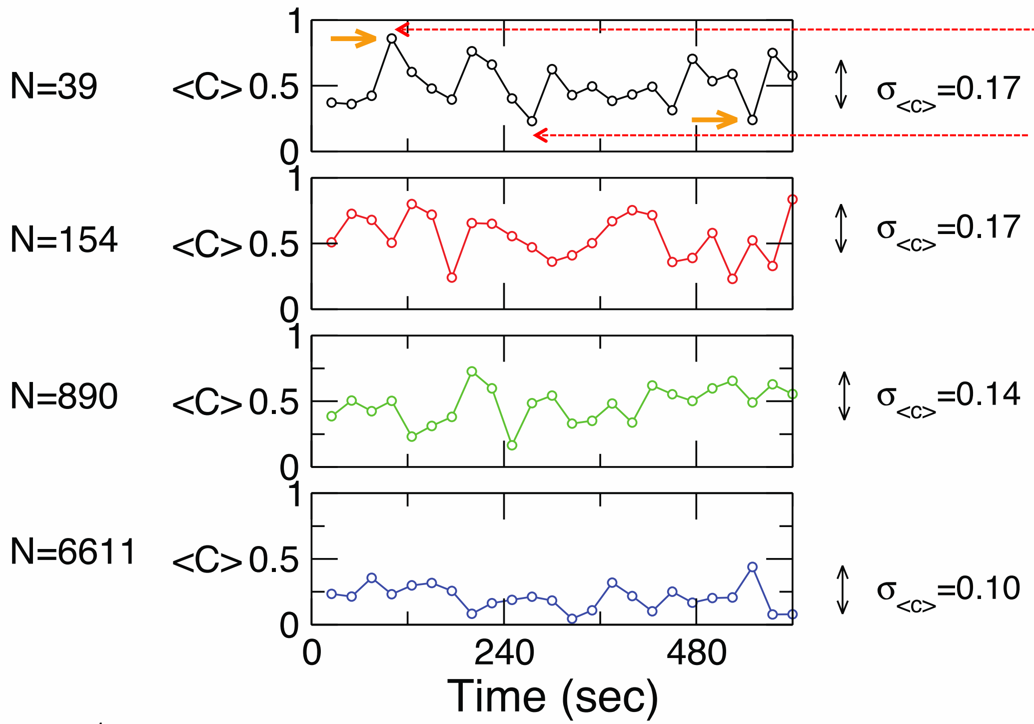
The variance of the temporal fluctuations is independent of the ROI size.

○ variance of the fluctuations computed for each of thirty five ROI

□ variance of the fluctuations computed for randomized data

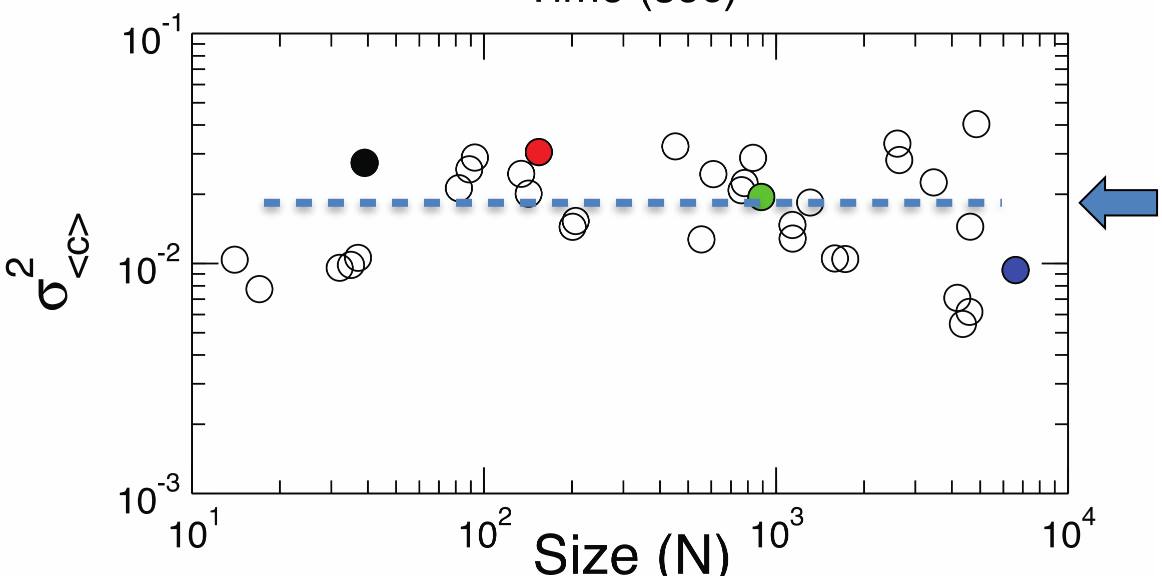
Chialvo DR & Fraiman D. (2010)

Consequences of the Increase in Correlation Length: Anomalous scaling of the time dependent correlations



Peaks of high correlation

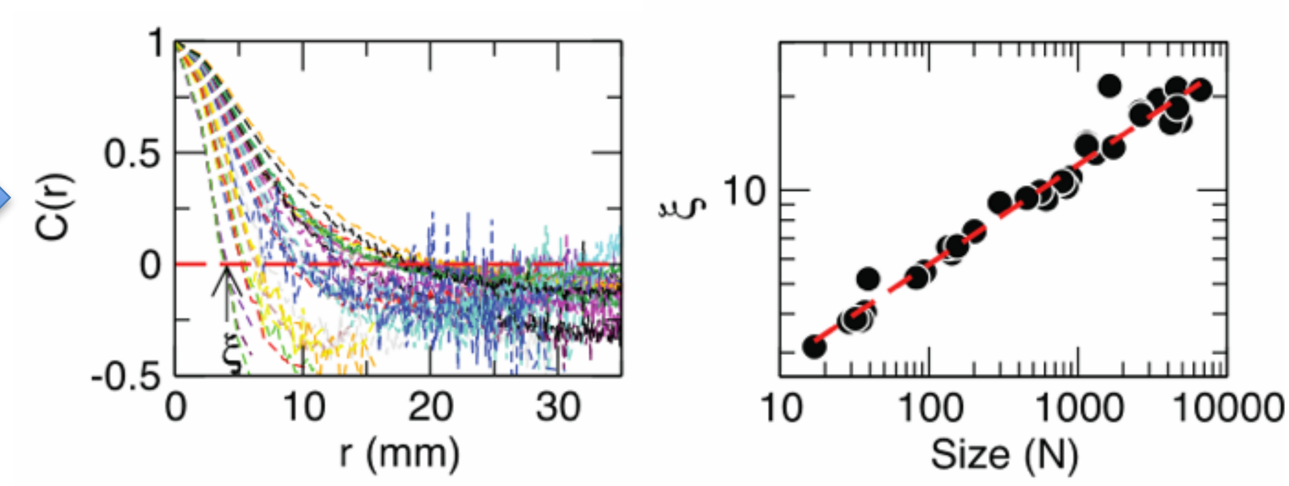
Valleys of low correlation



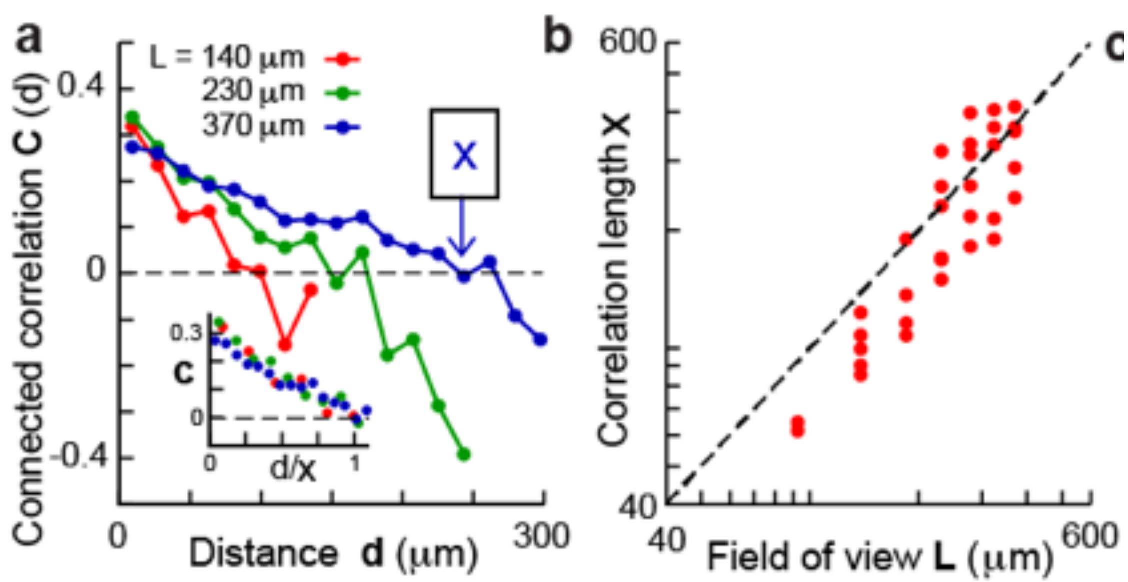
The variance of the correlations is **independent** of the ROI size correlation length: at criticality, it increases with system size

Data from human fMRI

(Fraiman & Chialvo, 2011)



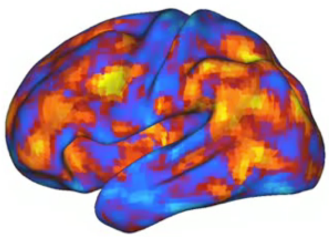
Data from optogenetic
2P recording in behaving
mice AI cortex
Plenz & Chialvo, 2017

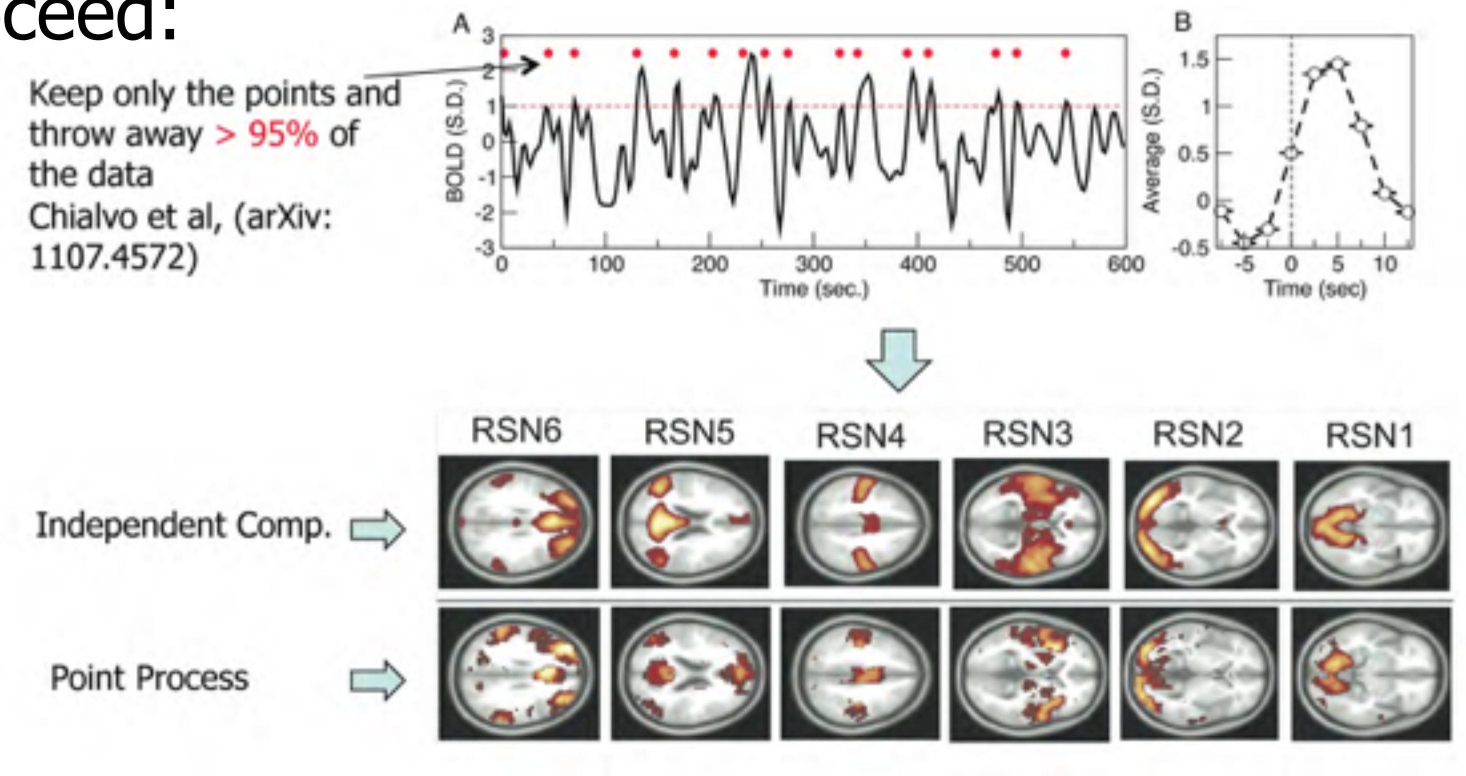


Brain "meteorology" (searching for order in very large scale, fMRI)

First, get the instantaneous dynamics (peaks)

how we proceed:



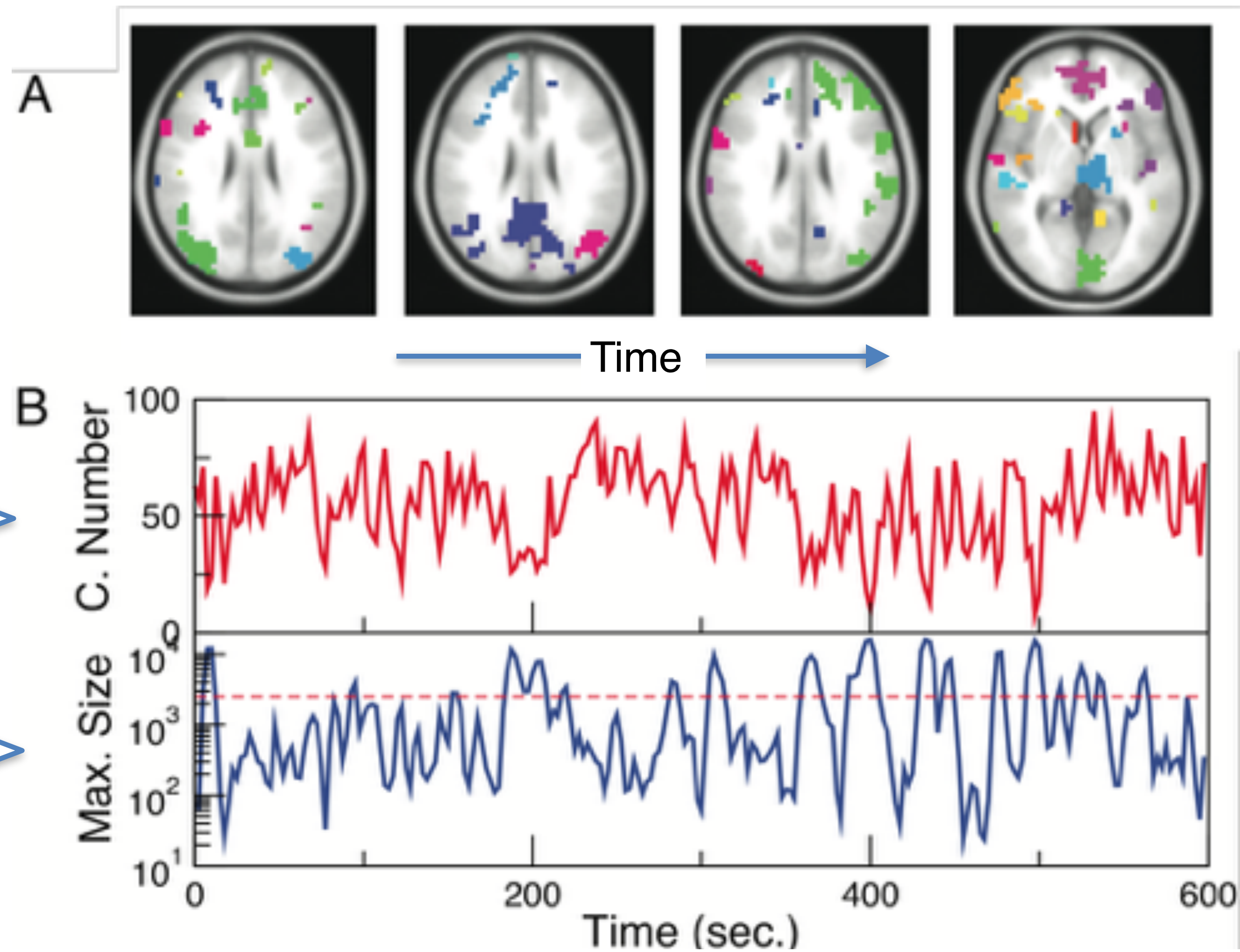


Moral: large scale dynamics is preserved despite a huge data reduction (95%) most of the information is in the peaks.

Brain “meteorology”

Second, identify clusters of activity (like clouds in the sky)

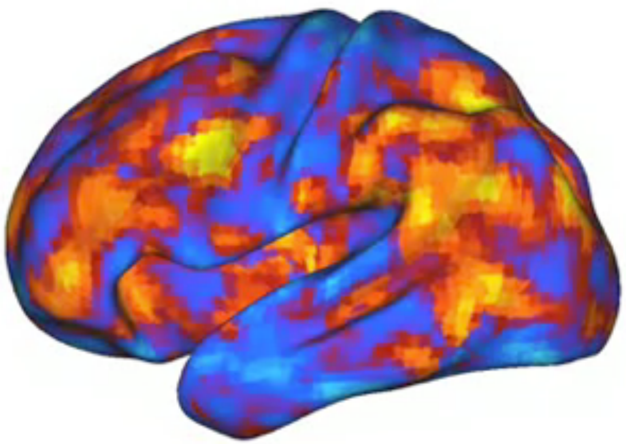
pixels in green belong to one cluster, blue to another, etc

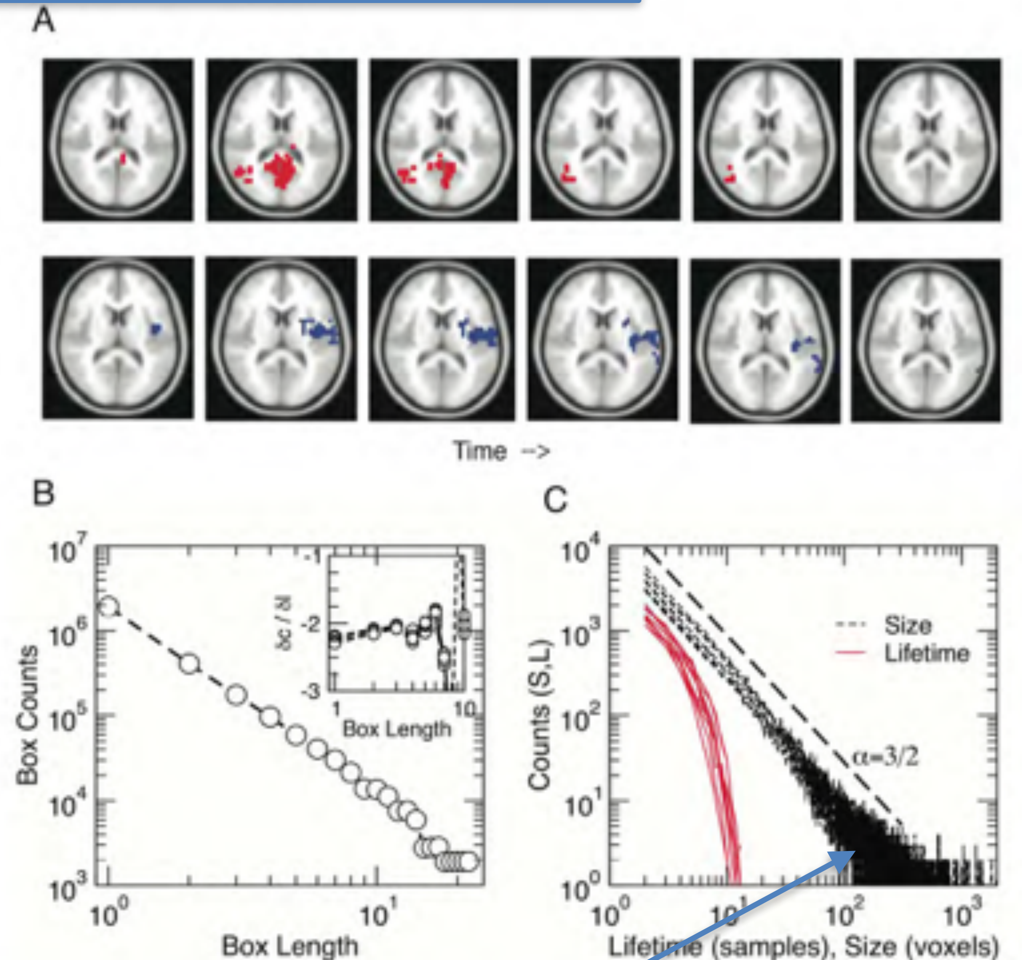


Number of clouds

Size of the largest cloud (sort of “order” parameter)

Third, identify spatiotemporal correlations (avalanches)





Fractal Dimension

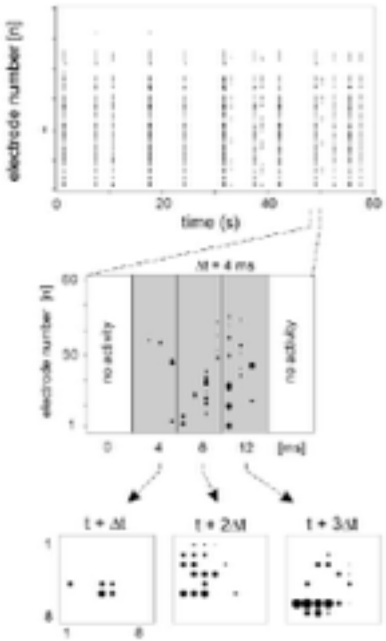
Lifetime PDF

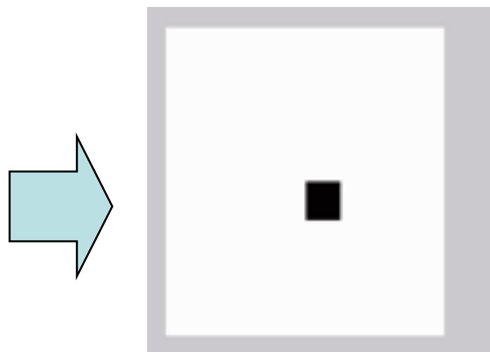
Size PDF

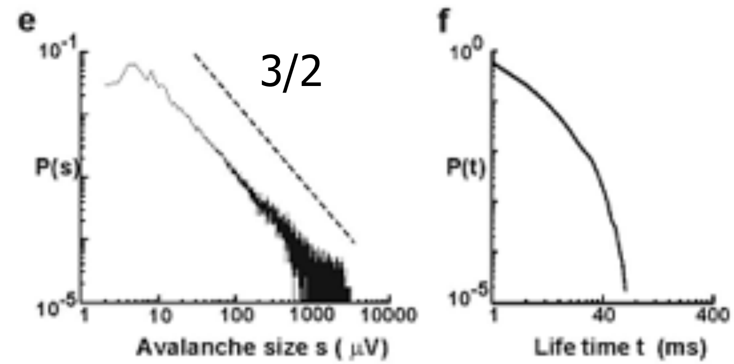
Avalanches of activity are scale free

From Tagliazucchi et al, Frontiers in Physiol. 2012.

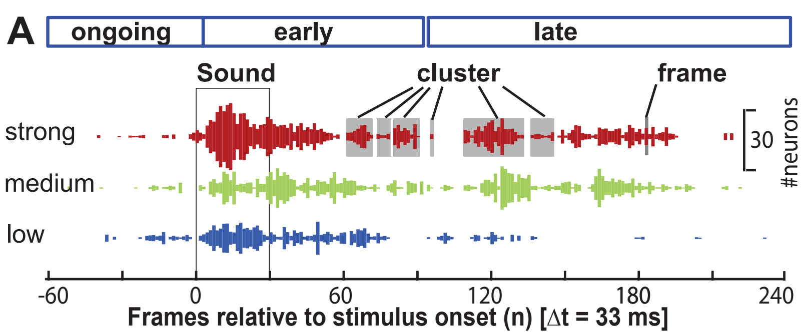
Identical avalanches were described in vivo & in vitro preps.

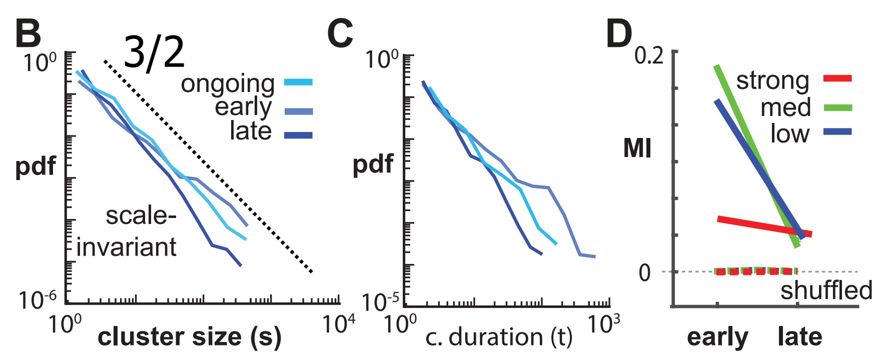






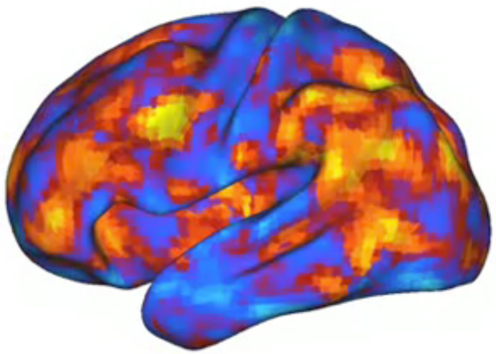
cultured rat cerebral cortex (Beggs & Plenz, 2003)

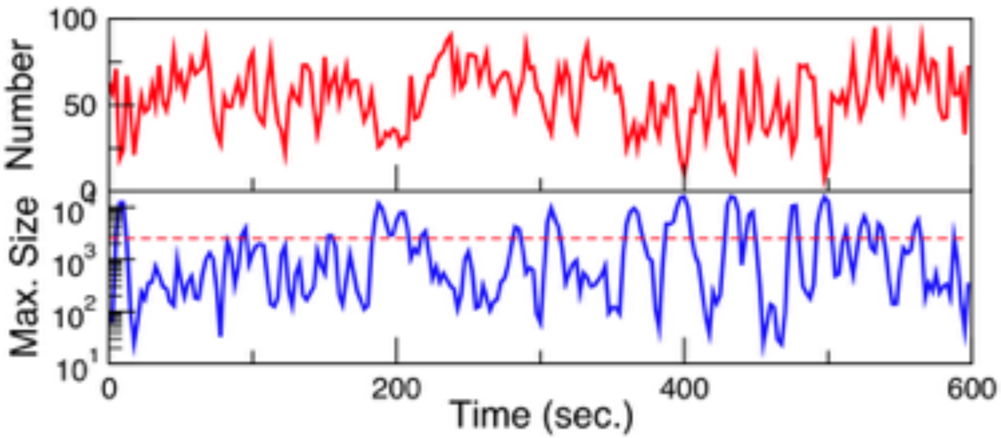




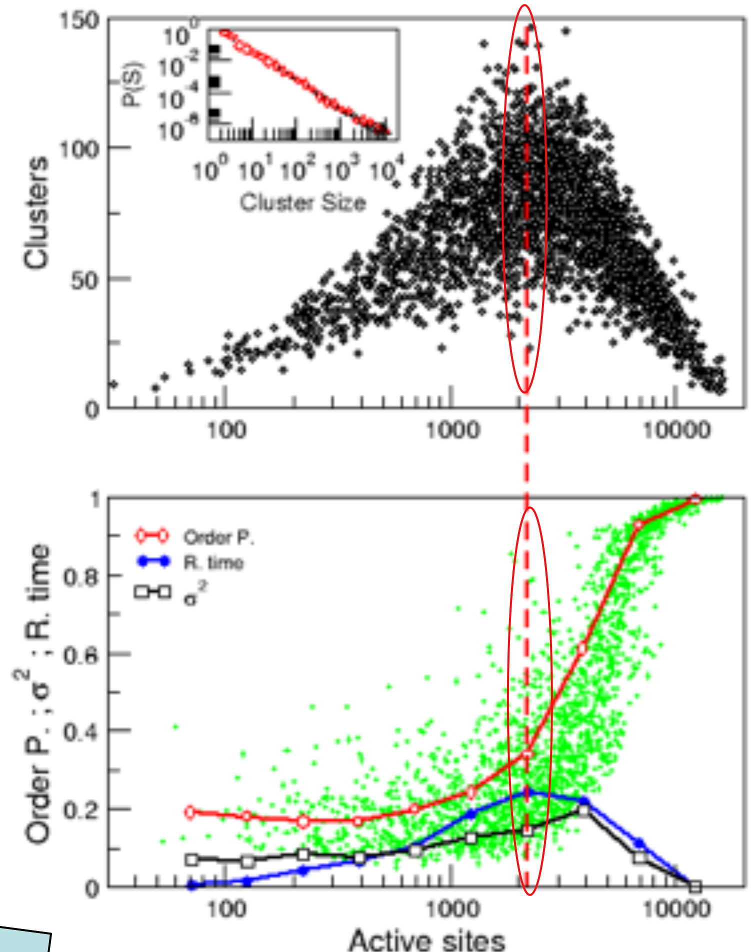
Optogenetic 2P recording in behaving mice AI cortex (Plenz & Chialvo,2017)

Fourth, check for "control" versus "order" parameter



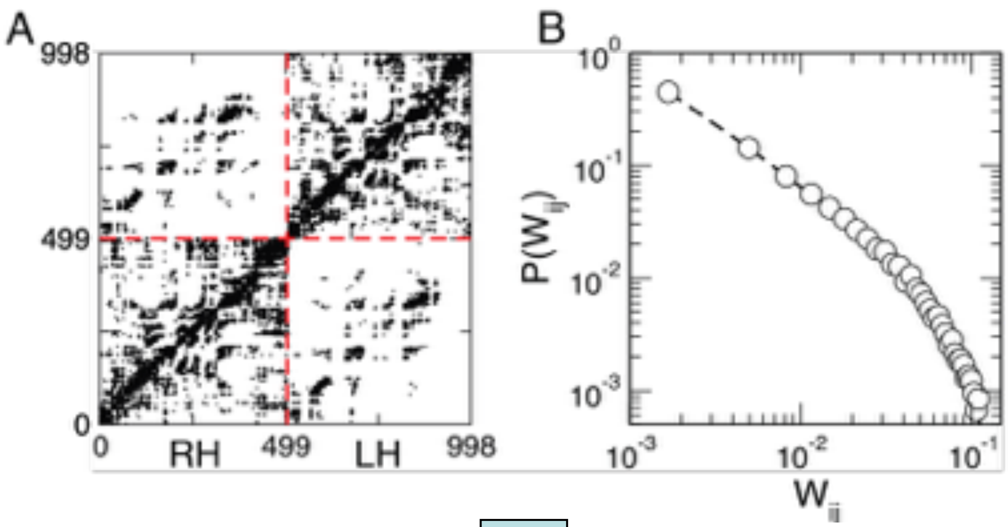


Spontaneous fluctuations of brain activity evolve as in a continuous phase transition, being most of the time at a regime with the largest variance



OK, lets do some modeling

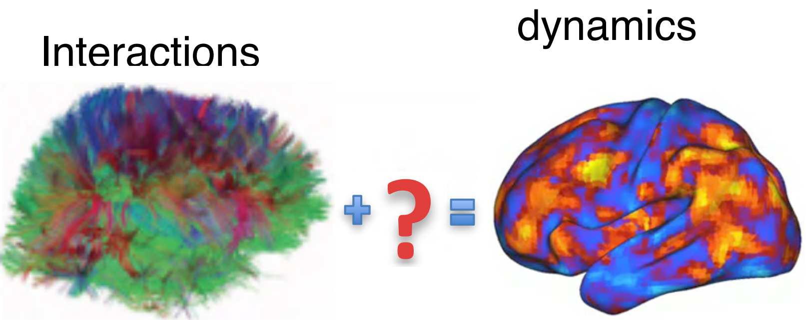
The *interactions* from the human connectome

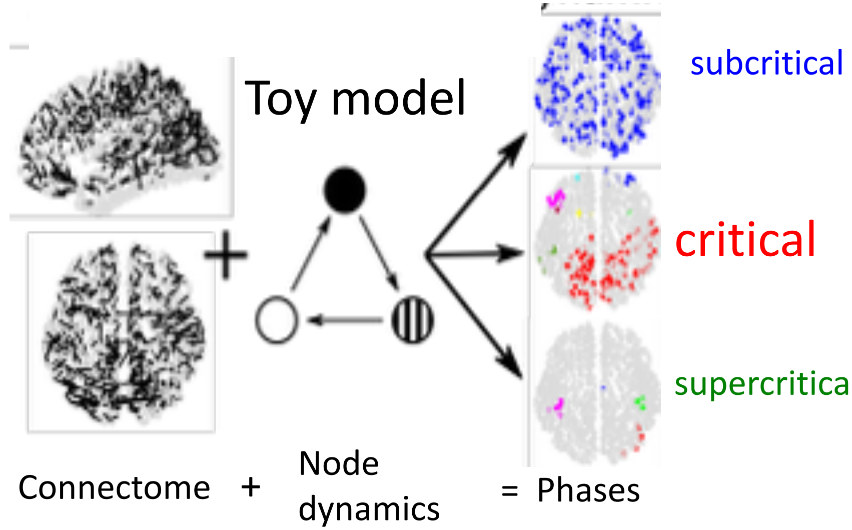


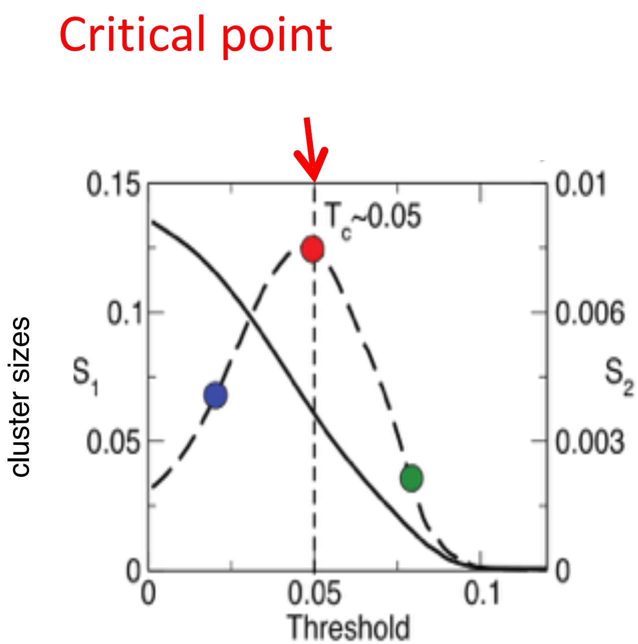
Plus some "simple" dynamics, actually (if universality applies) almost any nonlinear rule must give the exact same result…

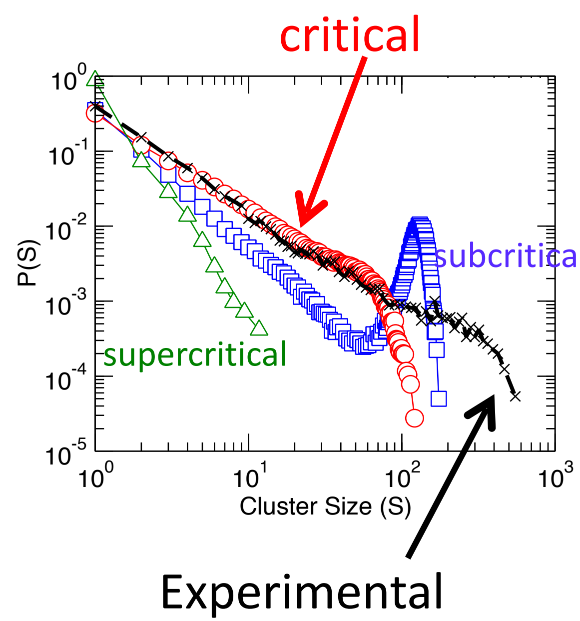
-Haimovici A, et al. "Brain organization into resting state networks emerges from the connectome at criticality". PRL (2013).

Getting the experimental *correlations* from the *interactions* ("Connectome")



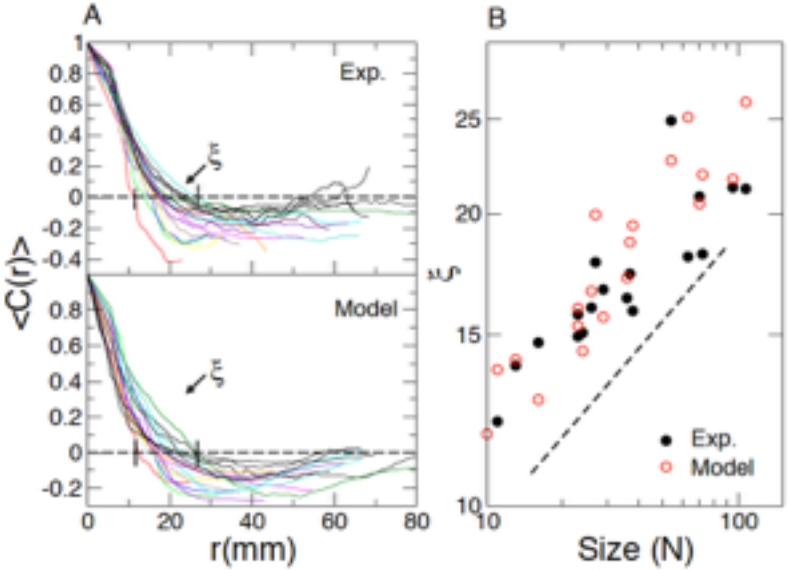




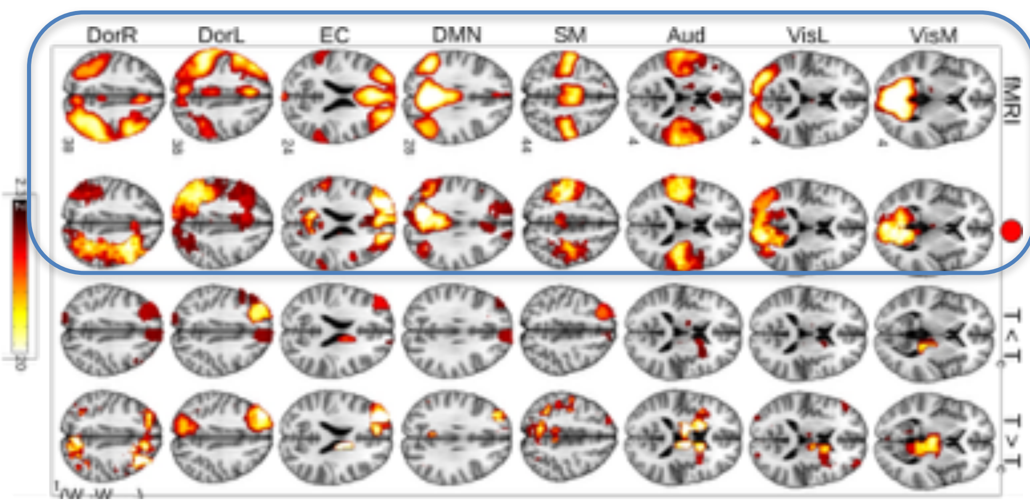


From Haimovici et al, Phys. Rev. Letters 2013.

Getting the same *correlations* from the known *interactions* ("Connectome")



Correlation length *increases* with cluster size exactly as seen in the real brain experiments



Experimental results (real brains).

critical

Sub critical

Super critical

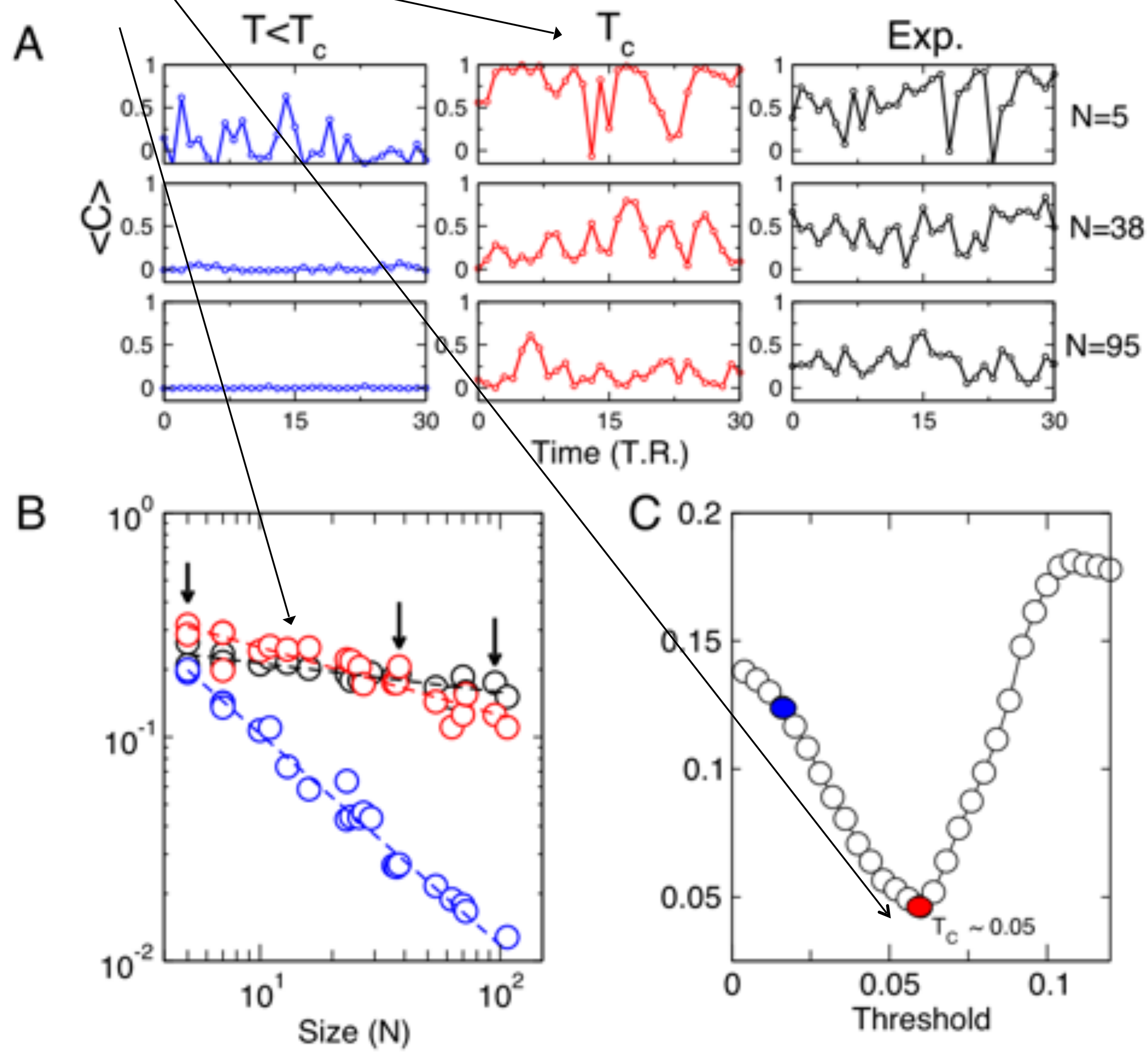
model

Only at *criticality* the model replicates the exp. data

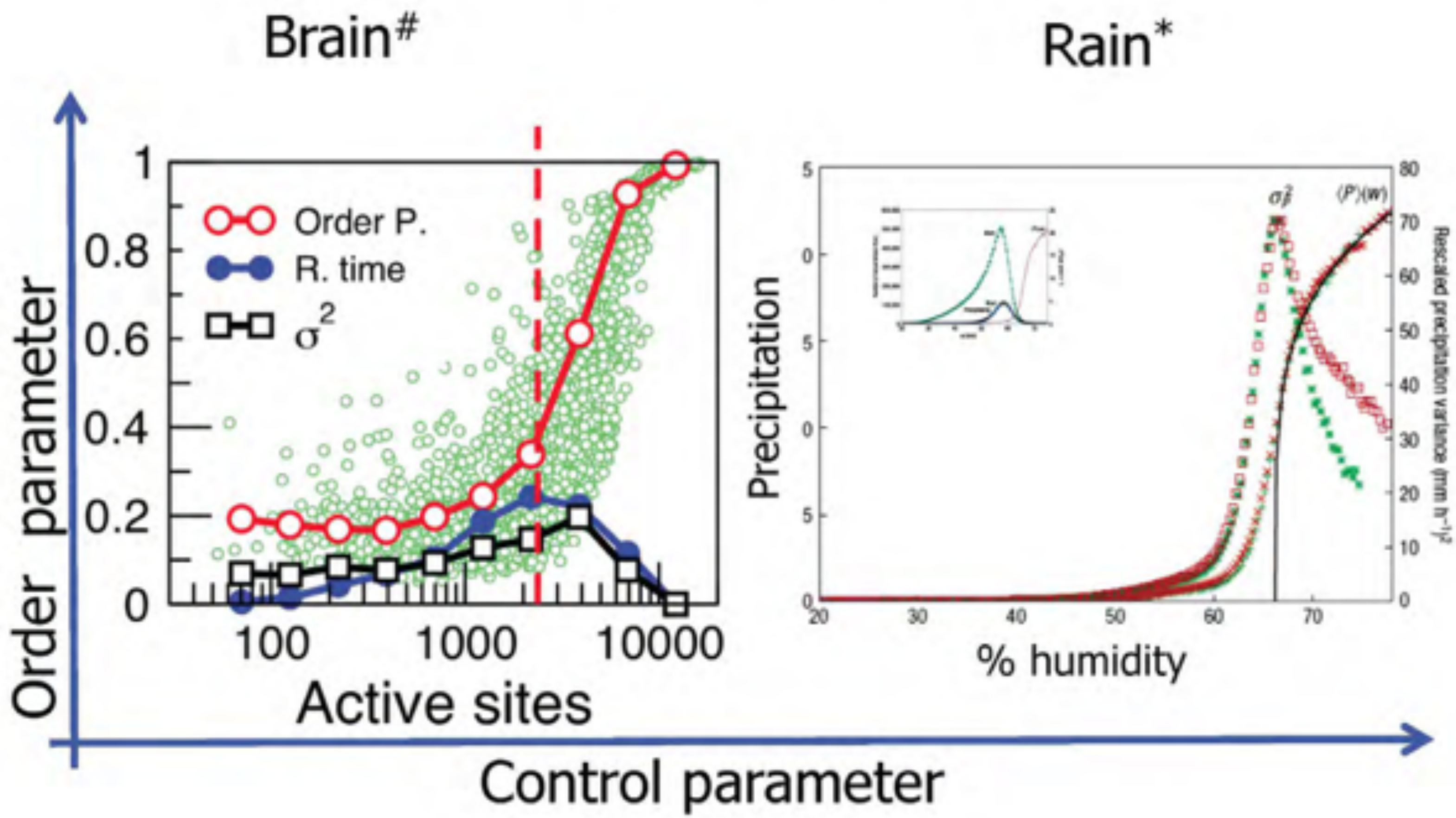
From Haimovici et al, Phys. Rev. Letters 2013.

The experimental dynamics is replicated only at criticality

Anomalous scaling of short term correlations



-Haimovici A, et al. Brain organization into resting state networks emerges from the connectome at criticality. PRL (2013).



*Peters & Neelin, Nature Phys. (2006).

Tagliazucchi et al, Frontiers (2012).

30

Summary

1- Some general properties, expected near the critical point of a continuous phase transition, are seen in fMRI brain data:

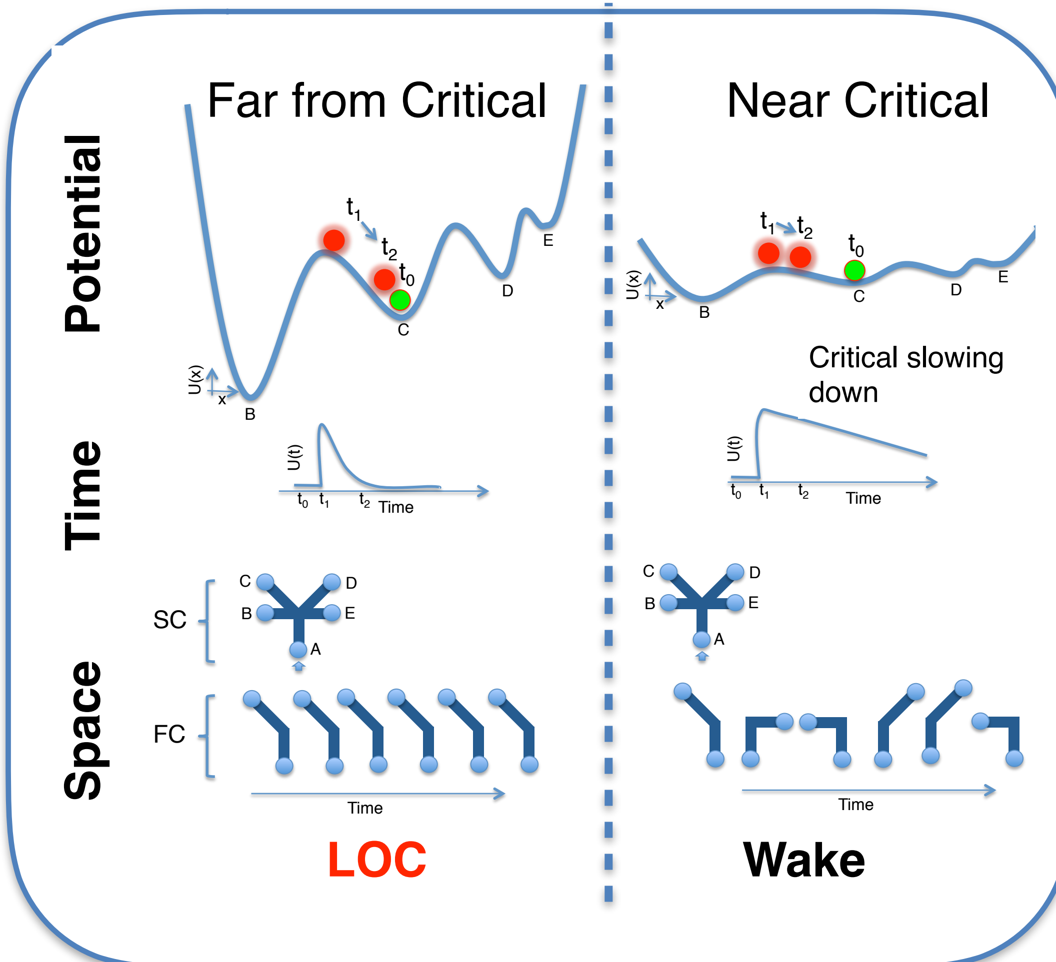
- ✓ Long range correlations in space and time.
- ✓ Correlation length scales with system size
- ✓ Anomalous scaling of the variance of the fluctuations
- ✓ Variance of the order parameter peaks at the critical point (susceptibility)
- ✓ Scaling in the clusters size distribution
- ✓ Scaling of avalanches sizes distribution

2- A model based on the brain connectivity replicates the observations ONLY at criticality, implying that "connectivity" is not enough to understand the dynamics.

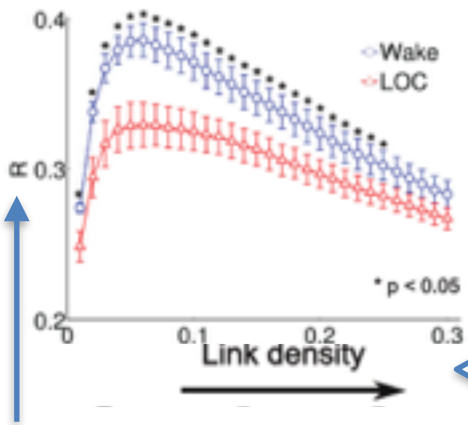
3- Despite 1 & 2 no theory is at hand to formally explain how the brain does it…

OK, the data shows the brain is critical while conscious…

How brain correlations will be affected with lost of consciousness (LOC) (Propofol anaesthesia)

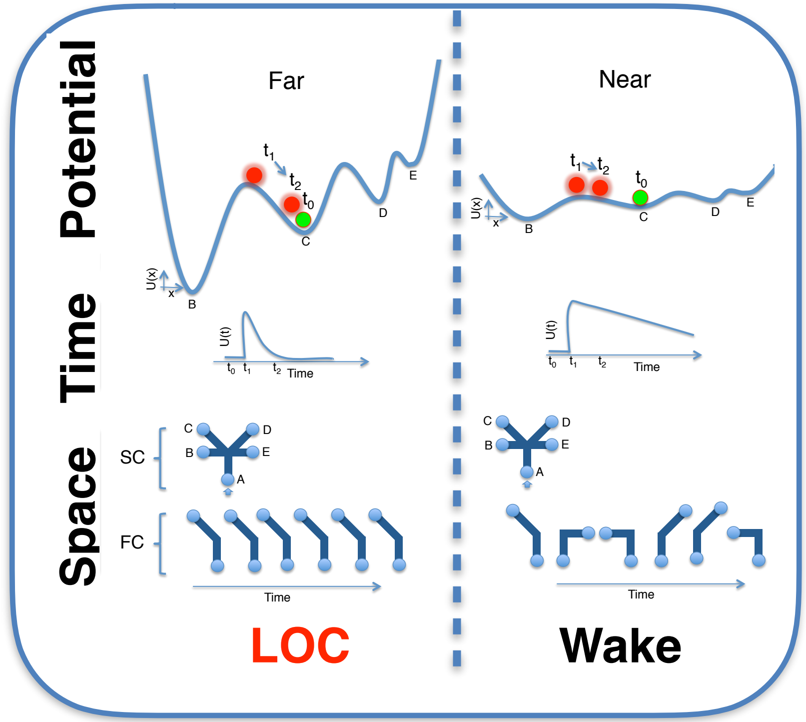


With lost of consciousness (LOC) correlations shifted as predicted



R~ FC/SC
(Ratio between number of observed paths over all posible paths)

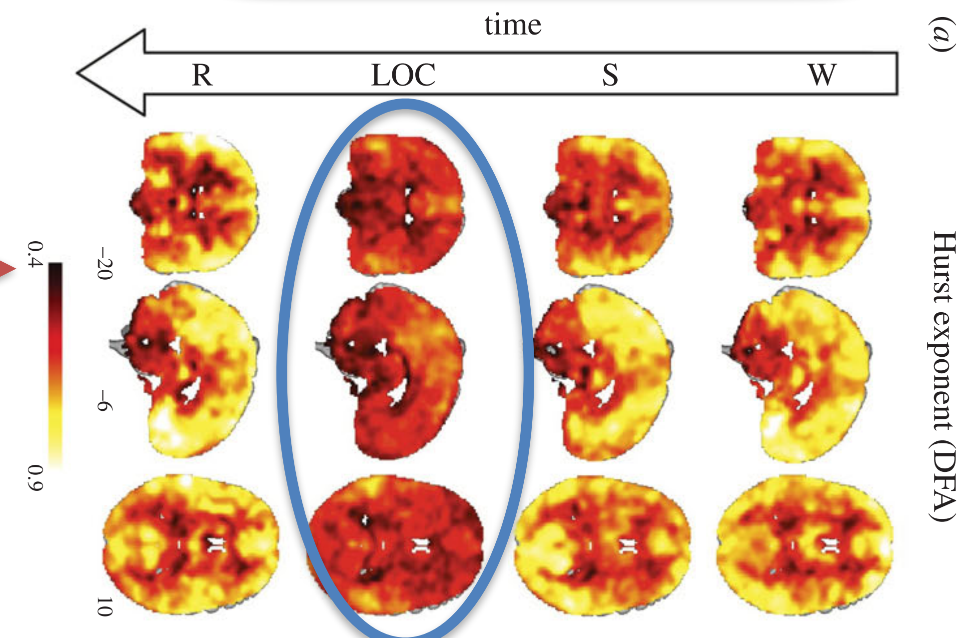
- Divorce of spatial *correlations* from *interactions*



- long-range *temporal correlations*

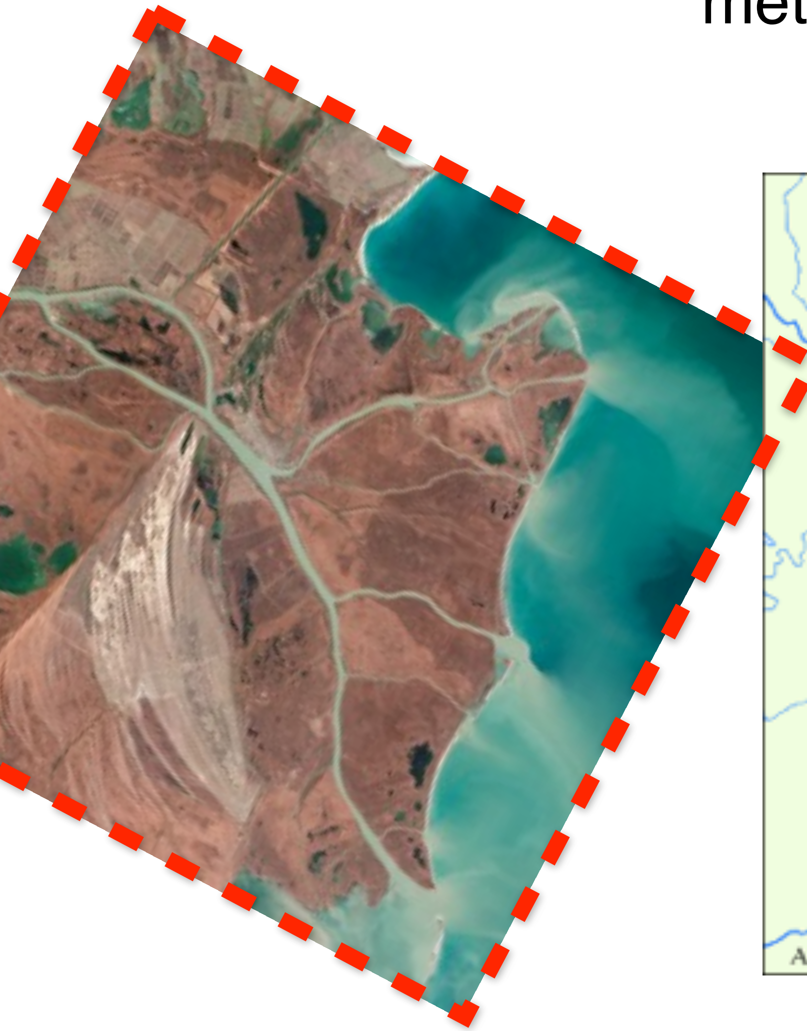
white noise (α ~ 0.5)

pink noise (α ~ 1)



Journal of the Royal Society Interface (2016).

The Danubio metaphor



The Danubio equivalent to the brain connectome

Third lecture

Outline

-Why life is always found near criticality? (a 10 minutes manifesto for the non-cognoscenti on “Not too rigid, neither very flexible”)

-We apply these ideas to:

- Brains (results on critical brain dynamics)

Today

- Proteins (finite size scaling analysis on NMR data from the PDB database) (Ph.D thesis of Y.T. Tang. Physical Review Letters 118, 088102, 2017)

- Mitochondria (critical fusion-fision balance of the mitochondrial network) 15 min. (with N&E Zamponi et al, Nature Sci. Reports 8, 363, 2018)

-Summary & questions

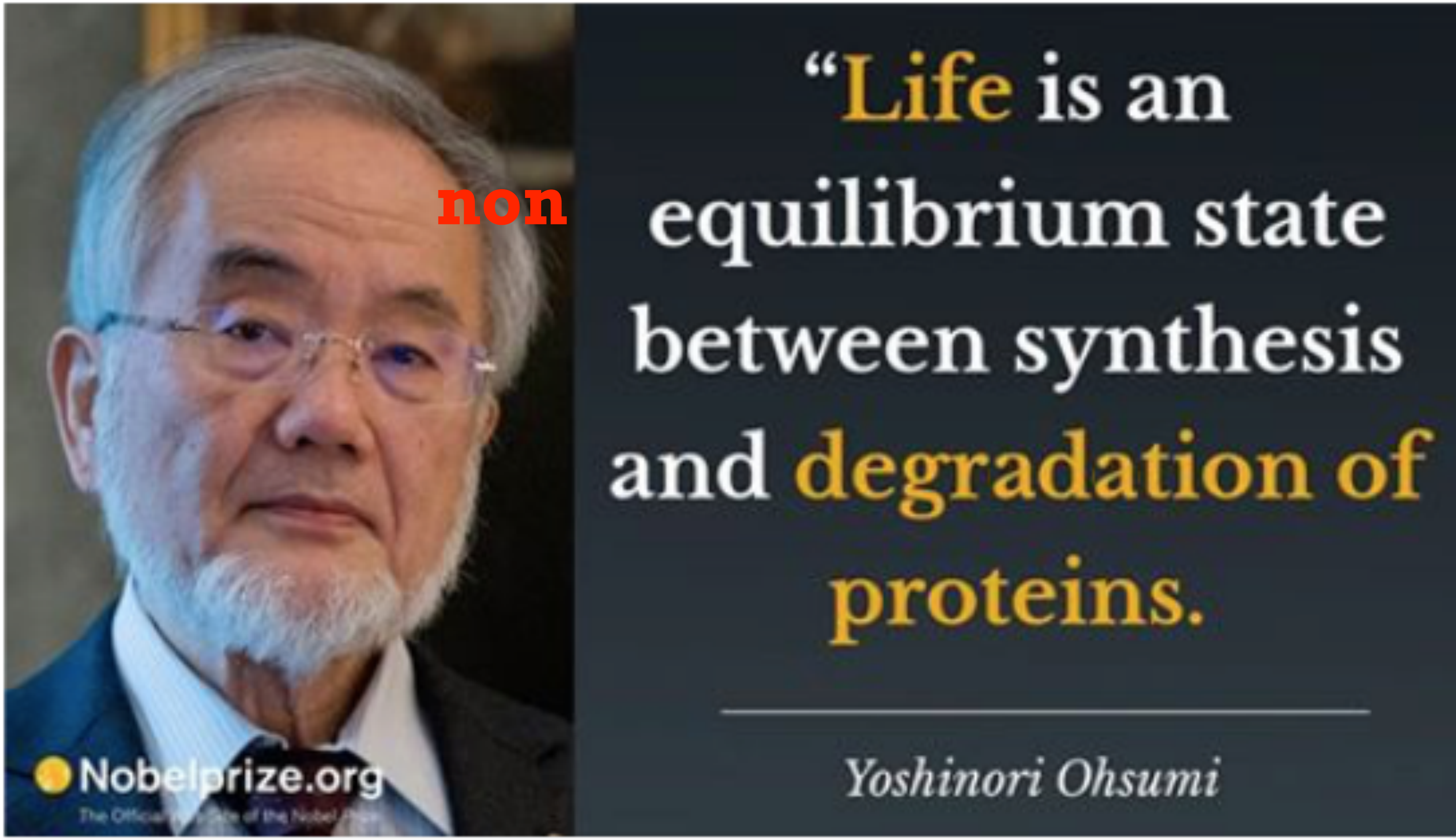
PRL 118, 088102 (2017) PHYSICAL REVIEW LETTERS week ending 24 FEBRUARY 2017

Critical Fluctuations in the Native State of Proteins

Qian-Yuan Tang,[1] Yang-Yang Zhang,[1] Jun Wang,[1,*] Wei Wang,[1,†] and Dante R. Chialvo[2,‡]
[1]*National Lab of Solid State Microstructure, Collaborative Innovation Center of Advanced Microstructures, and Department of Physics, Nanjing University, Nanjing 210093, China*

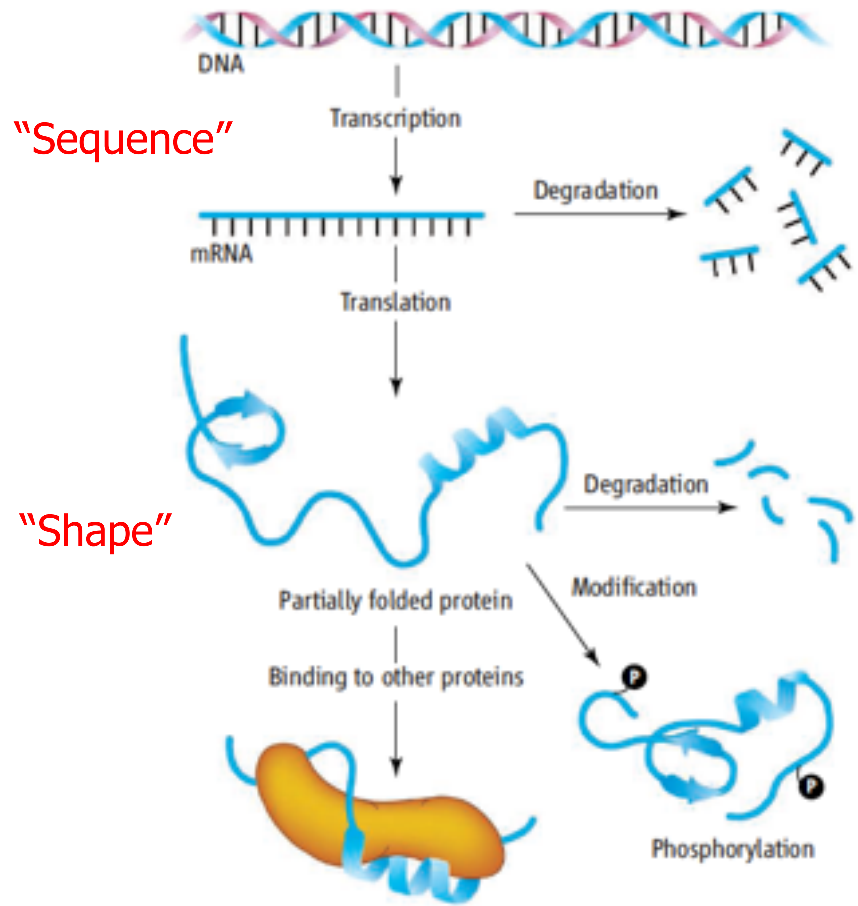
*with Q-Y Tang (Nanjing Univ., China)

*with Eliana Asciutto & Ignacio General (UNSAM, Argentina)



2016 Physiology and Medicine Nobel Prize

Proteins 101



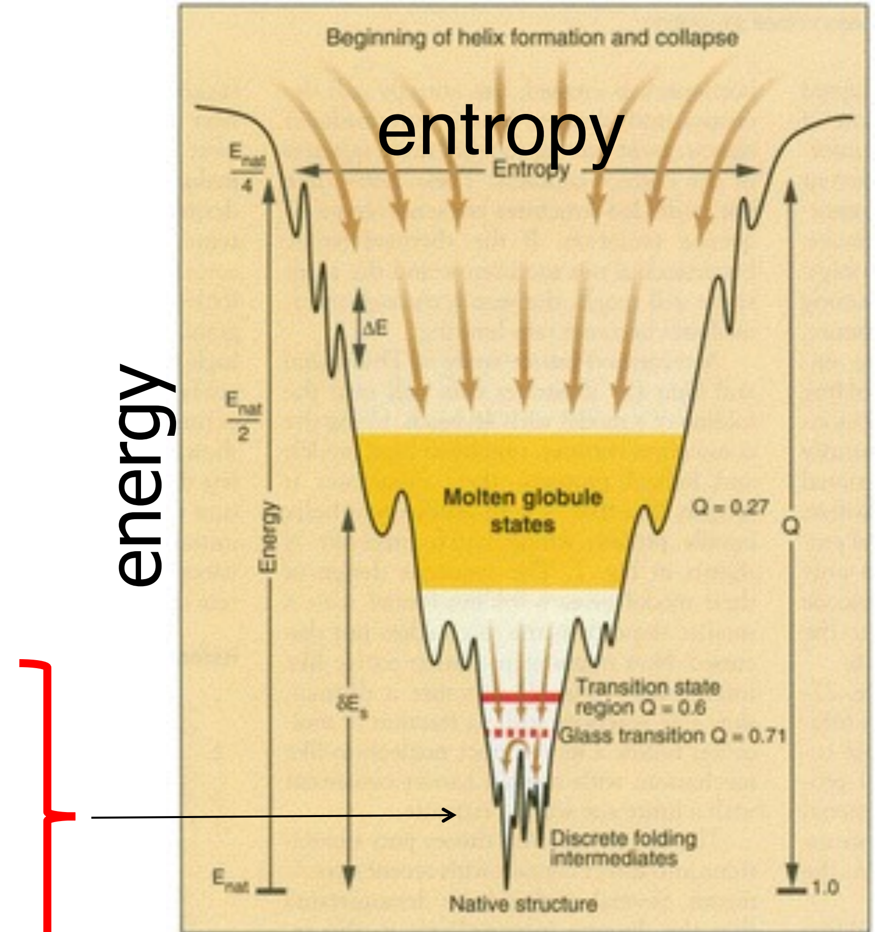


Fig. 1. Schematic of the folding funnel for a fast-folding 60-residue helical protein according to Onuchic *et al.* (*2*). The width of the funnel represents entropy, and depth, the energy. The flow of the molecule through the molten globule, folding bottleneck, or transition state ensemble and a glass transition region where discrete pathways emerge are indicated. The fraction of native contacts correctly made, *Q*, is indicated for each collection of states.

biology

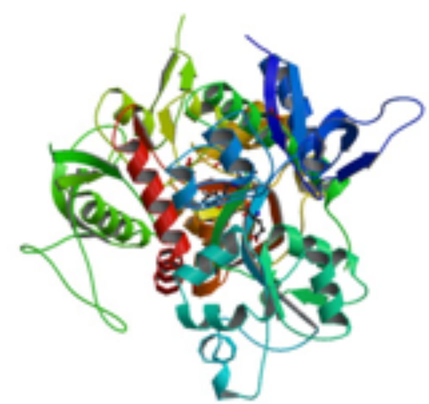
physics

Proteins 100: “sausage stuffer”

1-some sausages like water, others not
2- they have to mutually negotiate

3- fold (extremely fast)

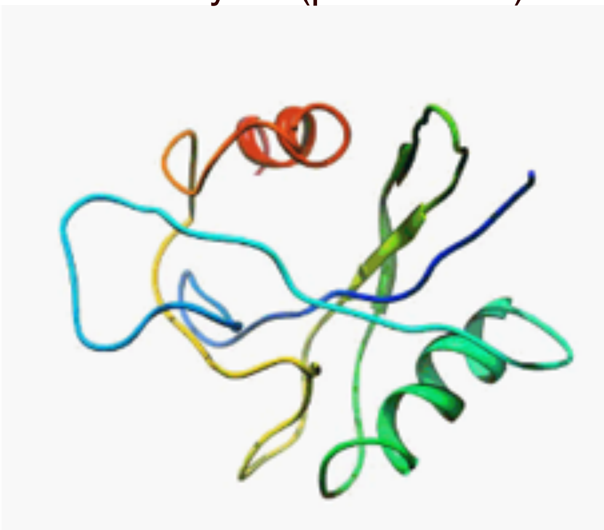
4- stay flexible



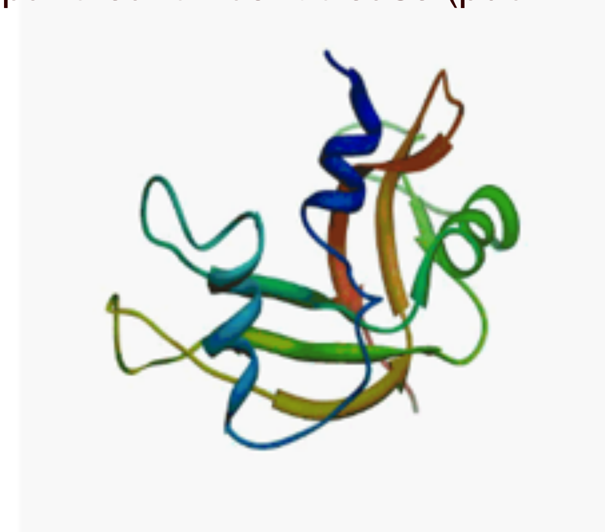
each sausage = one amino acid

Even today, when people think about protein structures, most sees them like that:

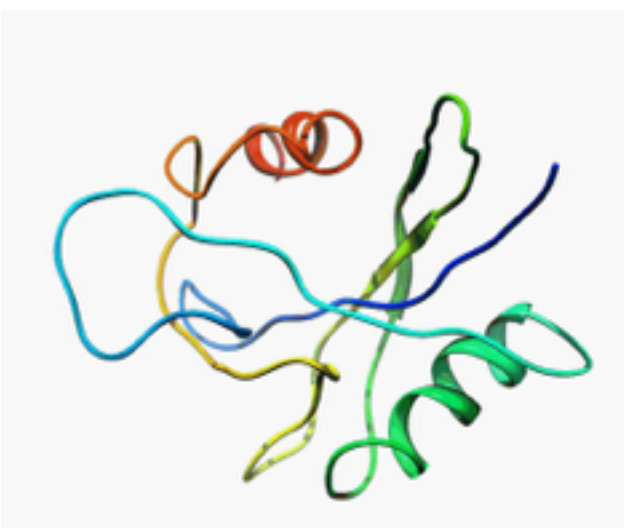
MutT enzyme (pdb: 1TUM)

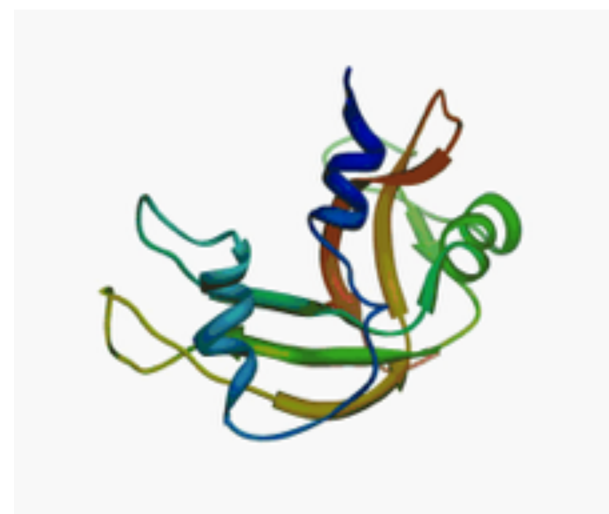


Human pancreatic ribonuclease (pdb: 2k11)



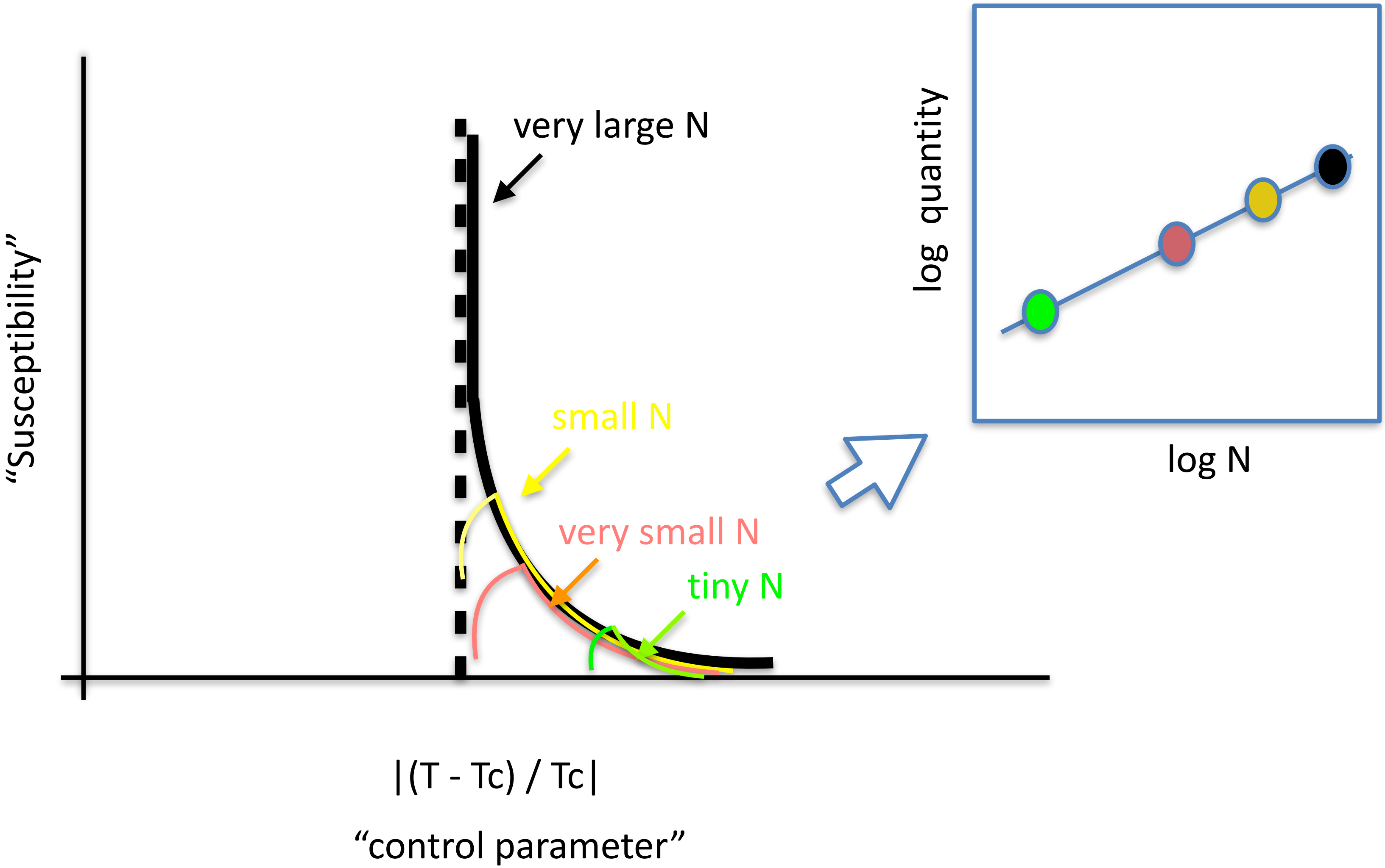
Indeed, proteins are ***flexible***, and their shape fluctuates:





Say something about correlation features of the protein fluctuations, using finite-size scaling

(getting it from a experiment with relatively small size N)



Type of data analyzed:

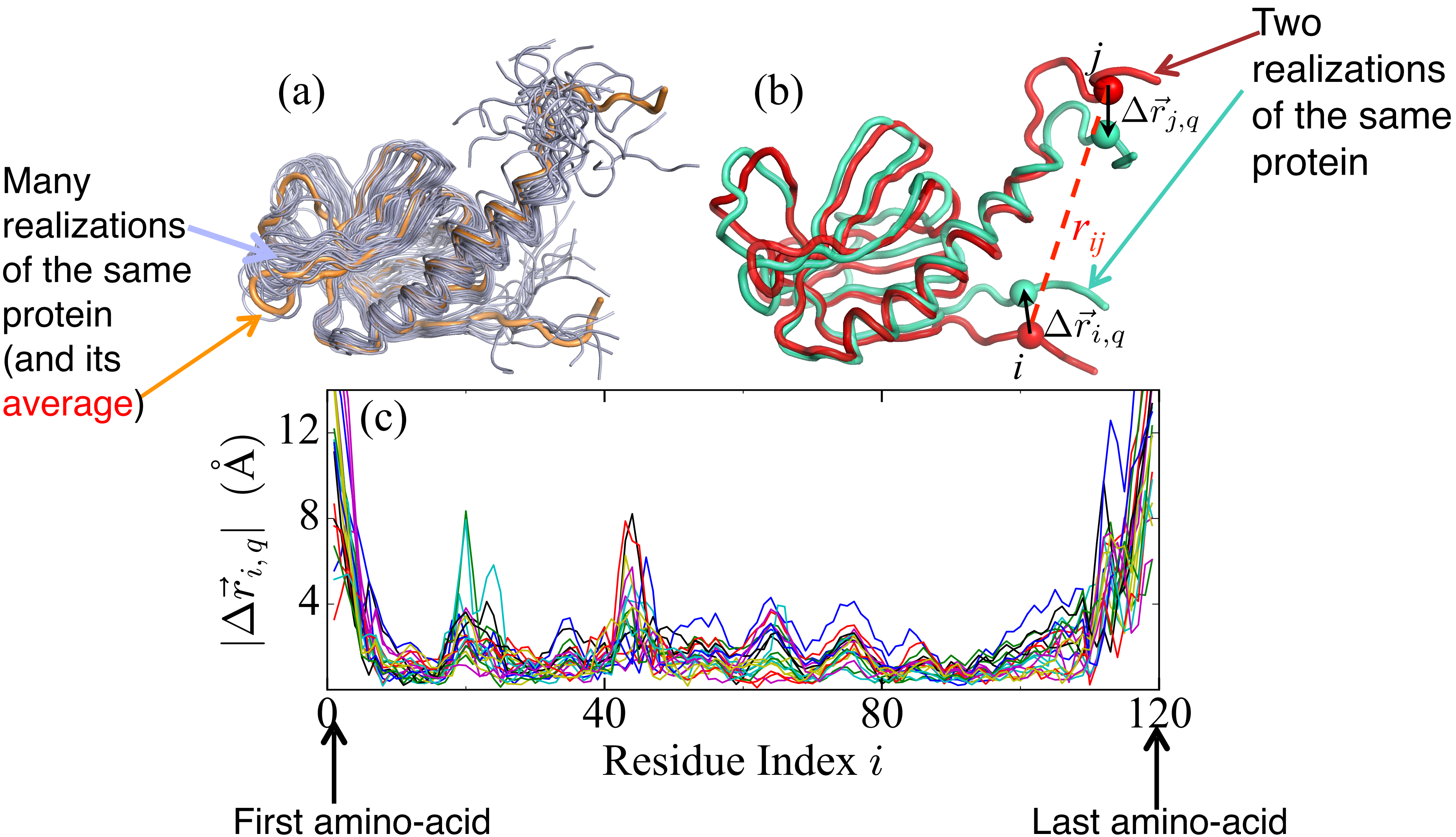
- We curated a data set including > 4000 proteins structures (ensembles from the Protein Data Bank)
- Include homo sapiens, bacteria, peptides,…
- Include only structures obtained from NMR experiments (solvent). [No membrane proteins]
- All proteins with more than 95% of the sequence-structure resolved.
- no more than 40% sequence similarity.

PRL **118**, 088102 (2017) PHYSICAL REVIEW LETTERS week ending 24 FEBRUARY 2017

Critical Fluctuations in the Native State of Proteins

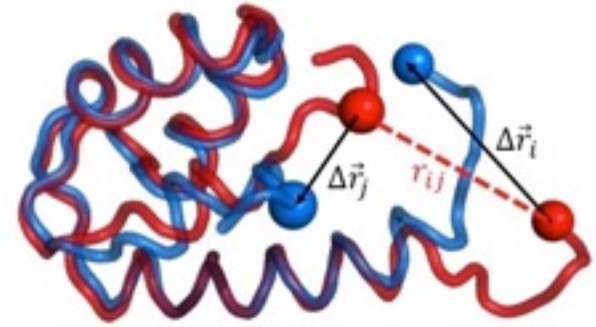
Qian-Yuan Tang,[1] Yang-Yang Zhang,[1] Jun Wang,[1,*] Wei Wang,[1,†] and Dante R. Chialvo[2,‡]
[1]*National Lab of Solid State Microstructure, Collaborative Innovation Center of Advanced Microstructures,*

Finite size scaling analysis of shape fluctuations



Fluctuation (for each realization) around the mean vs. position in the chain

Notation



- "i" : order of the amino-acid element in the chain
- "q": protein realizatdion (out of a ensemble of Q)

For the protein "q*":

- Amino-acid "i" coordinates: $\vec{r_i} = [x_i, y_i, z_i]$

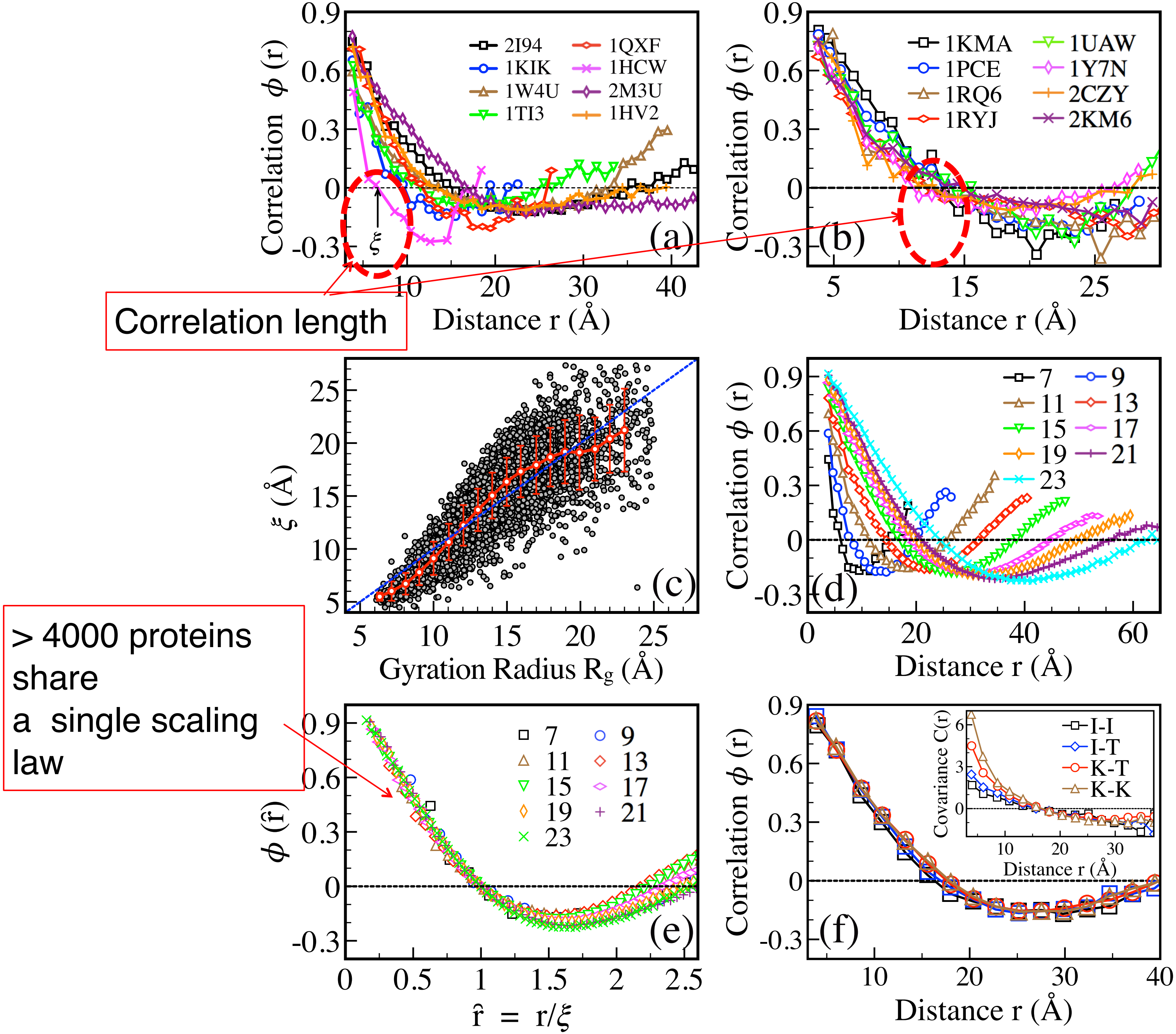
Connected Correlation Function

- Fluctuation around the mean of amino-acid "i": $\vec{\Delta r_i} = \vec{r_i} - \frac{1}{Q}\sum_{q=1}^{Q} \vec{r_{i,q}}$

  ○ Distance dependent covariance $C(r)$ and cross-correlations $\phi(r)$.

$$C(r) = \frac{\sum_{i\neq j}^{N} \vec{\Delta r_i}\cdot\vec{\Delta r_j}\,\boxed{\delta(r-r_{ij})}}{\sum_{i\neq j}^{N}\boxed{\delta(r-r_{ij})}} \qquad \phi_{ij} = \frac{\Delta\vec{r_i}\cdot\Delta\vec{r_j}}{\sqrt{(\Delta\vec{r_i}\cdot\Delta\vec{r_i})\cdot(\Delta\vec{r_j}\cdot\Delta\vec{r_j})}}$$

- Susceptibility: $\chi = \frac{1}{N}\sum_{i\neq j}^{N}\phi_{ij}\cdot\theta(\xi_\phi - r_{ij}).$
- "Size": N (length) R_g ; (Gyration Ratio).
- Shape factor: $s = Na^3/(L_a L_b L_c)$ <- pseudo control par.



Correlation length
> 4000 proteins share
a single scaling
law
(a)
(b)
(c)
(d)
(e)
(f)
Correlation φ (r)
Distance r (Å)
ξ
2I94
1KIK
1W4U
1TI3
1QXF
1HCW
2M3U
1HV2
1KMA
1PCE
1RQ6
1RYJ
1UAW
1Y7N
2CZY
2KM6
ξ (Å)
Gyration Radius R_g (Å)
7
9
11
13
15
17
19
21
23
φ (r̂)
r̂ = r/ξ
Covariance C(r)
I-I
I-T
K-T
K-K

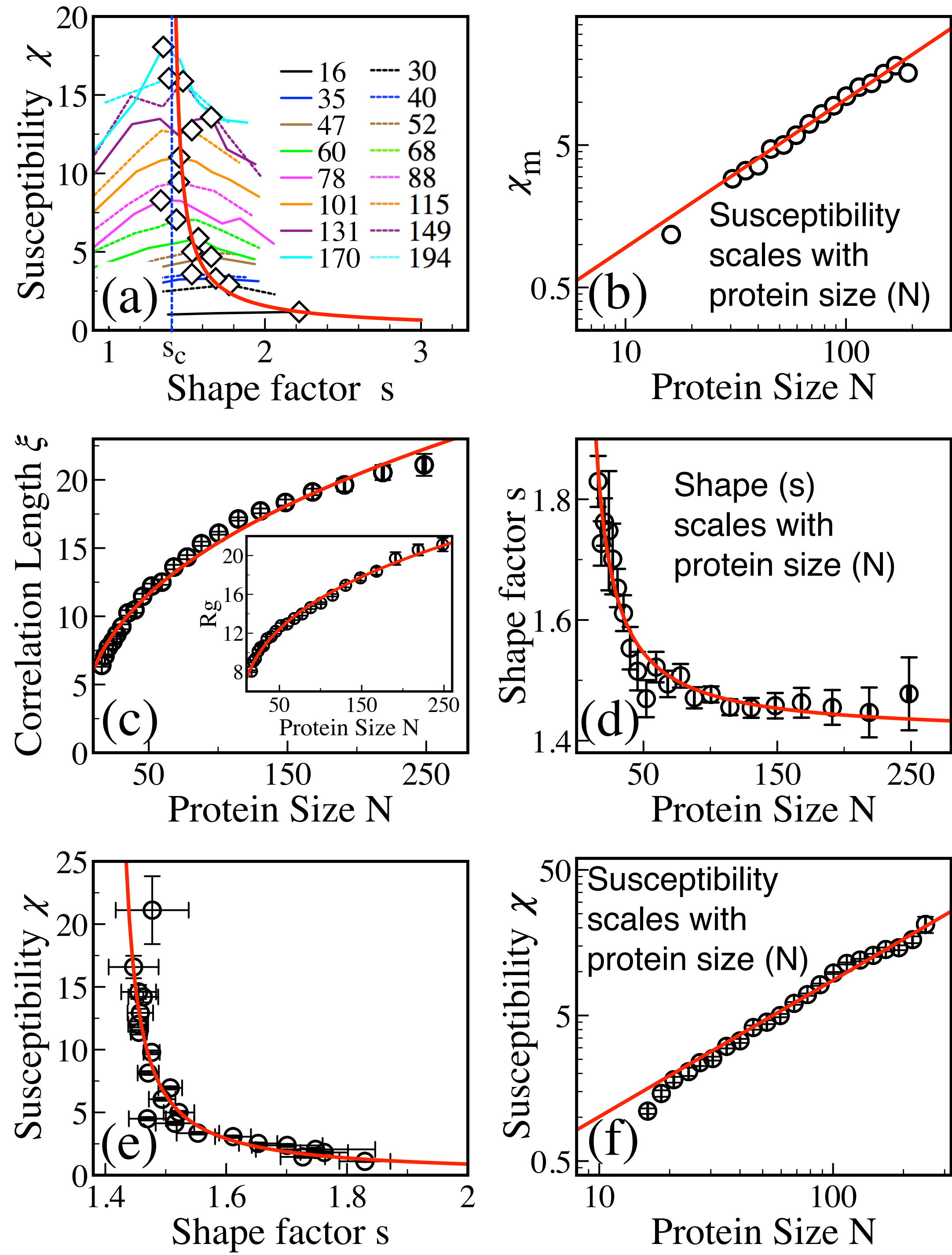
Finite-size scaling analysis

Correlation length scales with protein size (N)

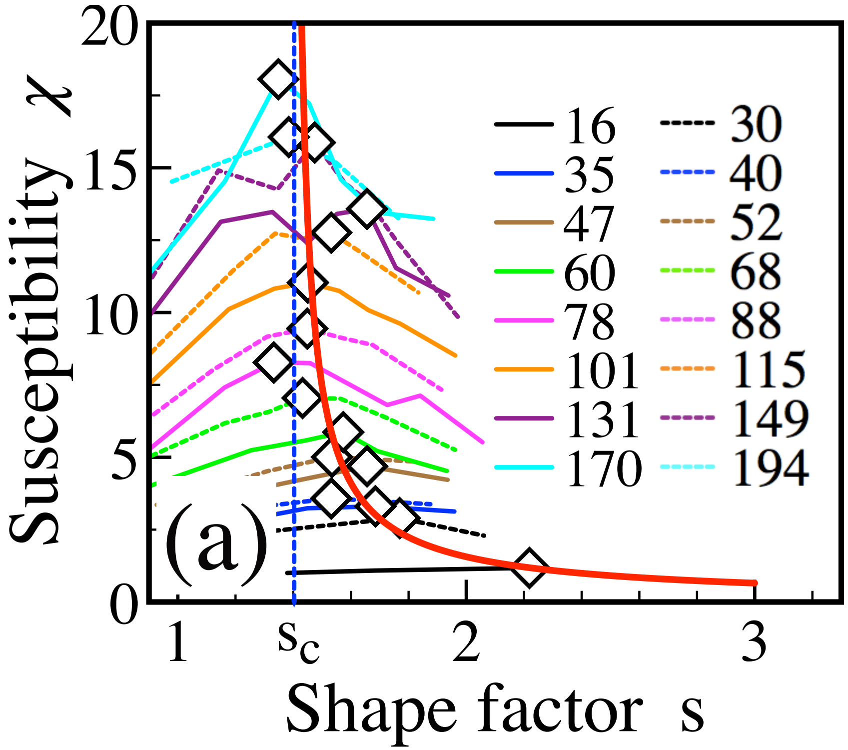
- Residue packing: $R_g \sim N^{1/3}$
- Correlation length: $\xi \sim R_g$
- Shape factor: $s \sim R_g^{-1} \sim N^{-1/3}$
- Susceptibility: $\chi \sim s^{-3} \sim R_g^3 \sim N$

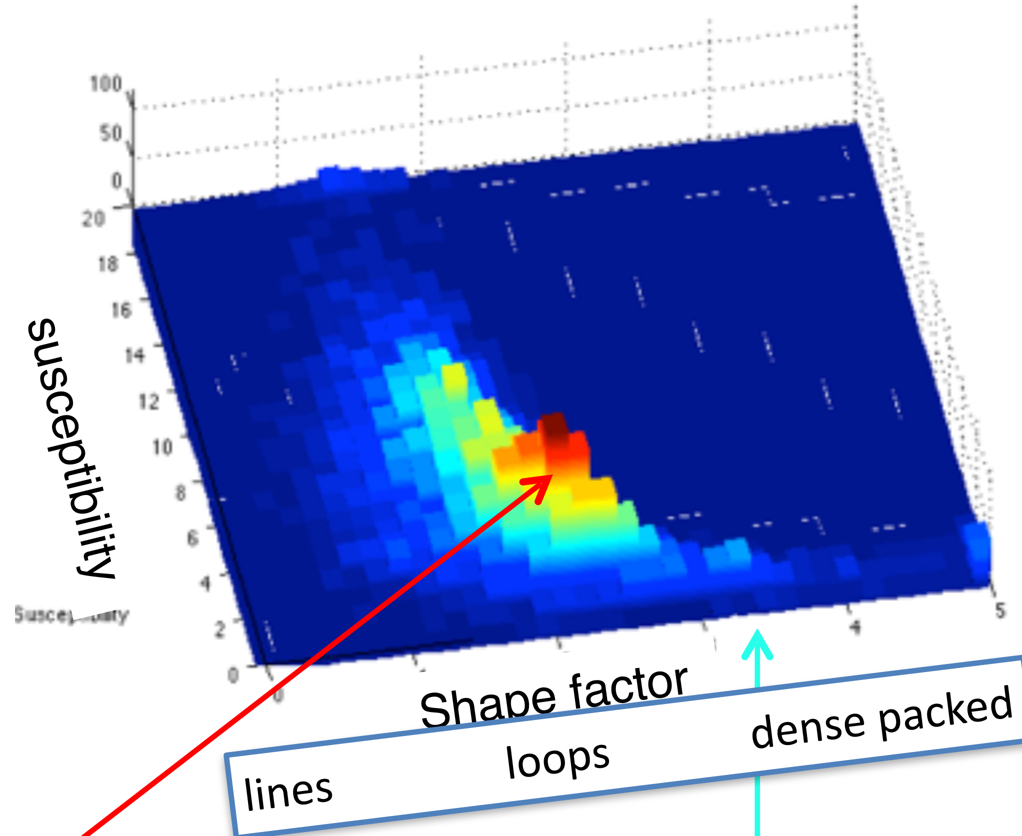
$$\chi_m \sim (s_m - s_c)^{-\gamma}$$

$$\chi_m \sim N^{\alpha\gamma/\nu}$$



- Highly *susceptible* proteins (i.e. critical) are more frequent

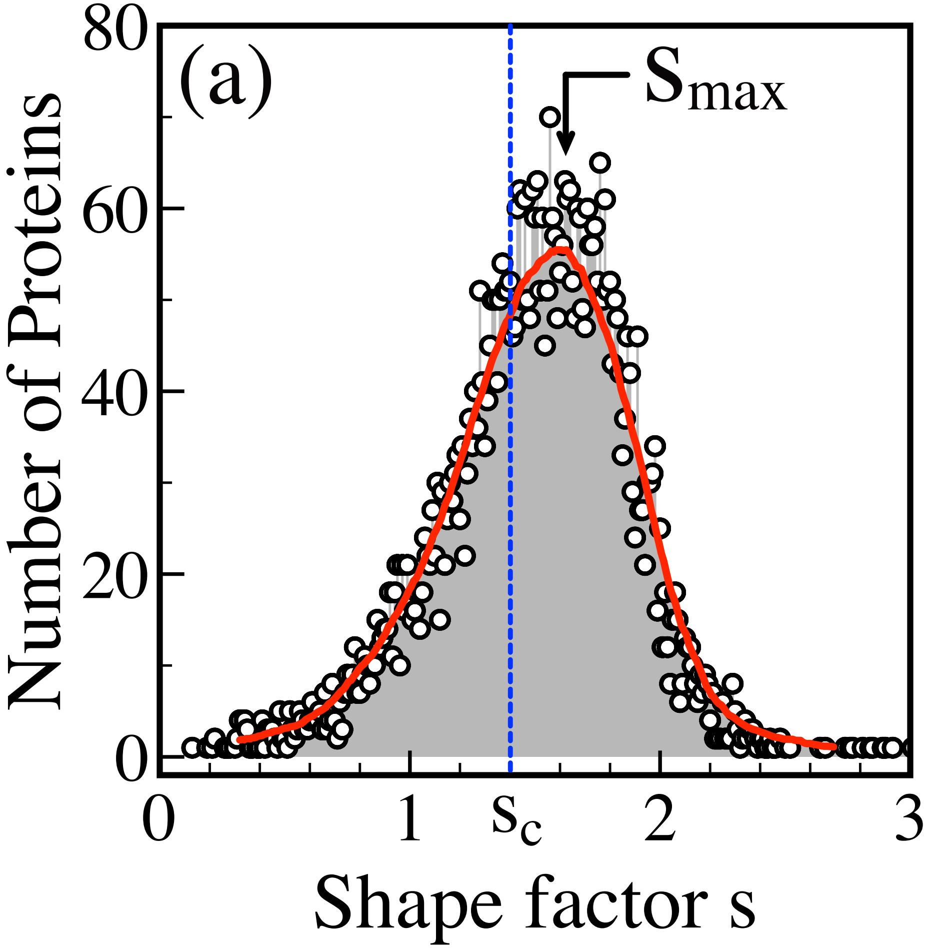


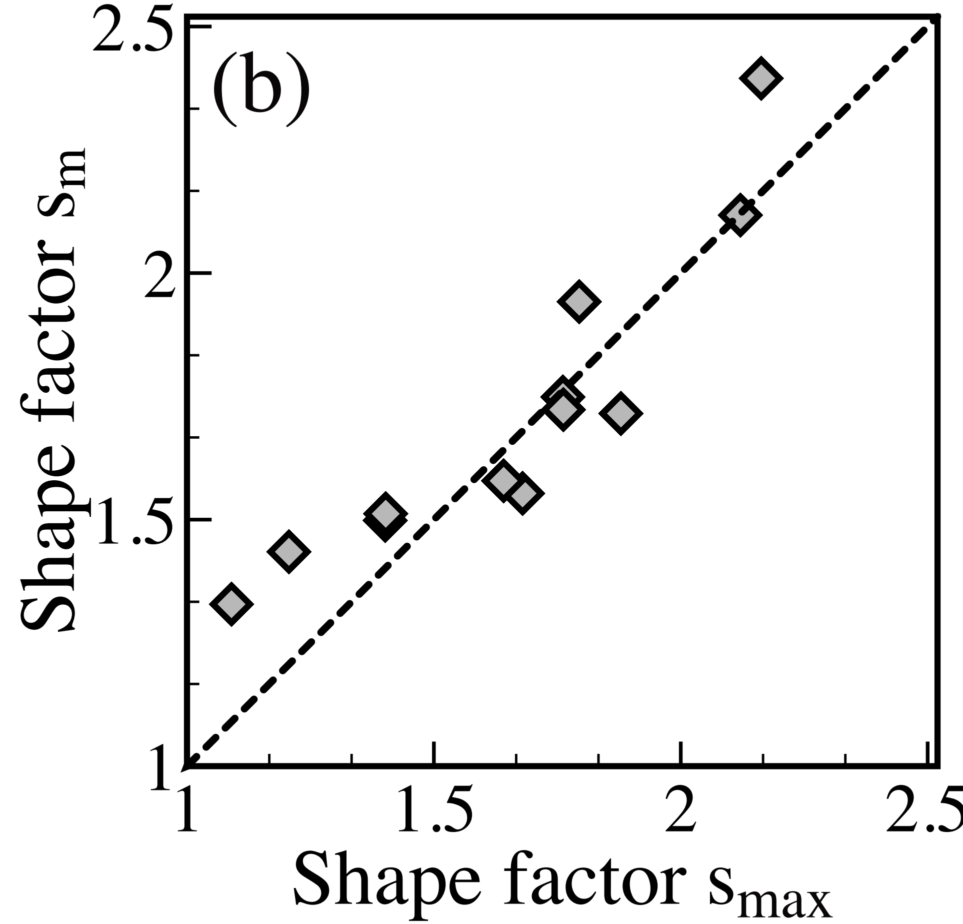


Sequences which are able to fold into a shape exhibiting high susceptibility are more frequent (evolutionary selected ?).

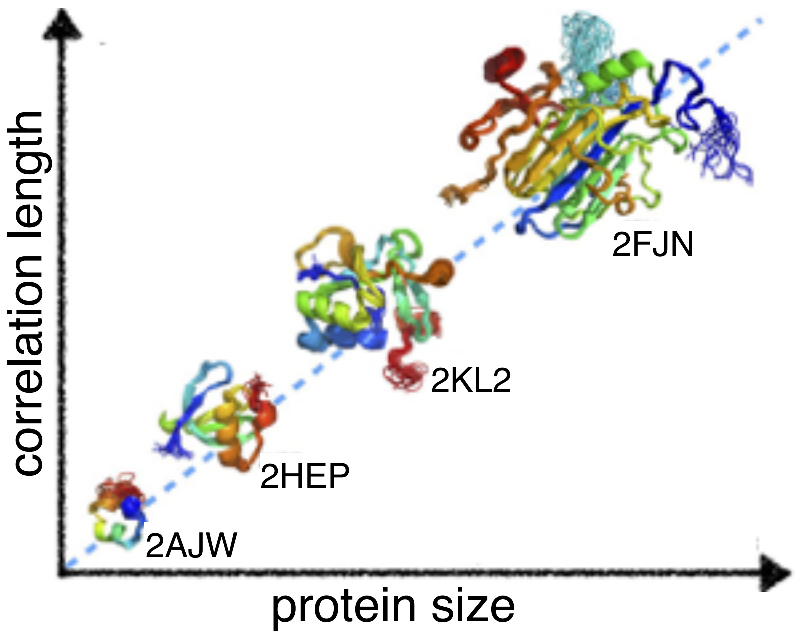
Other sequences (resulting in densely packed rigid proteins) are less frequent (not selected?.)

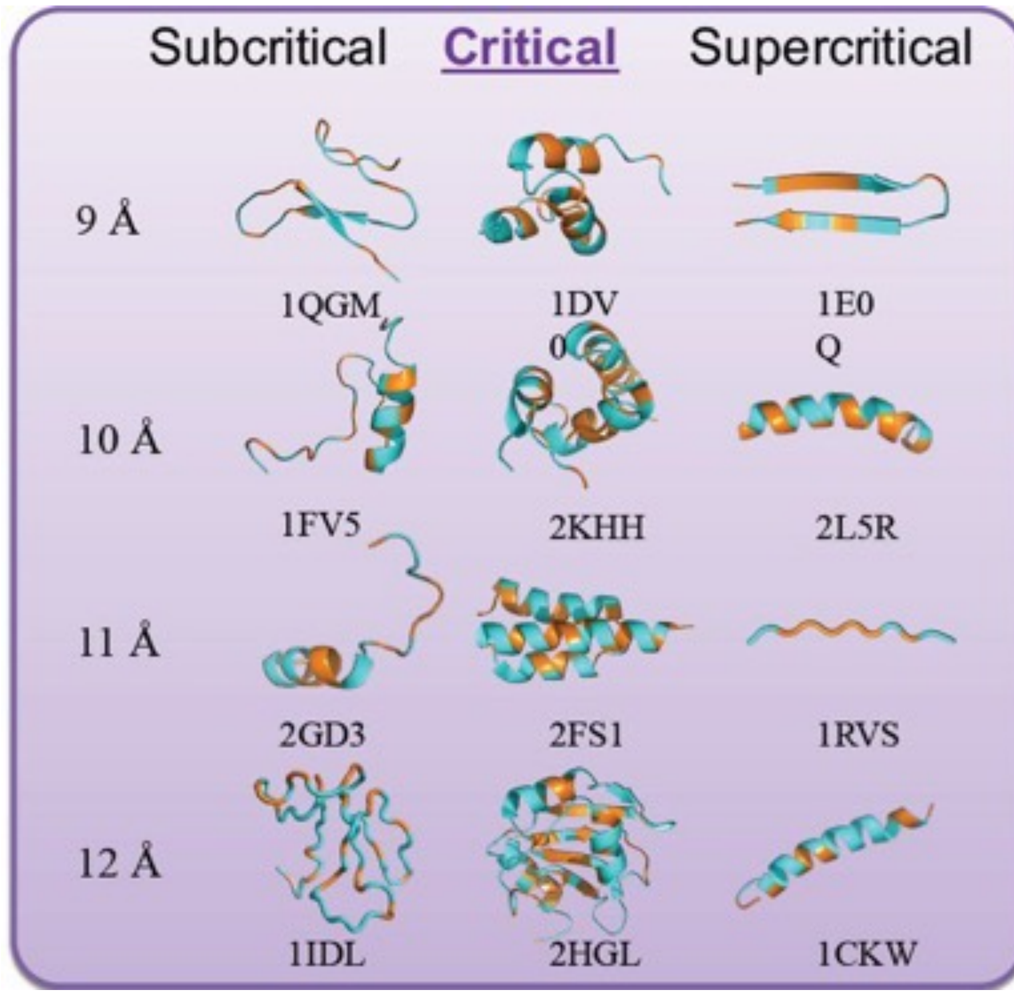
- The most frequent ***shapes*** are highly ***susceptible***





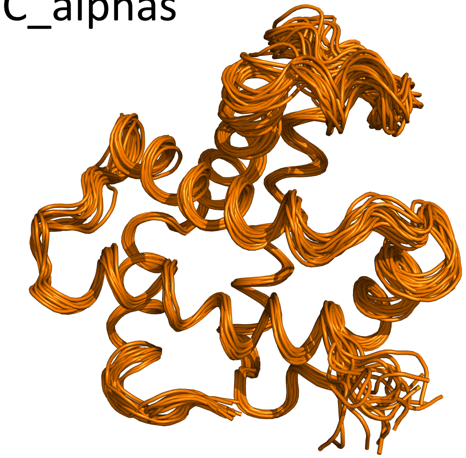
Don't trust the numbers, look if qualitatively makes sense





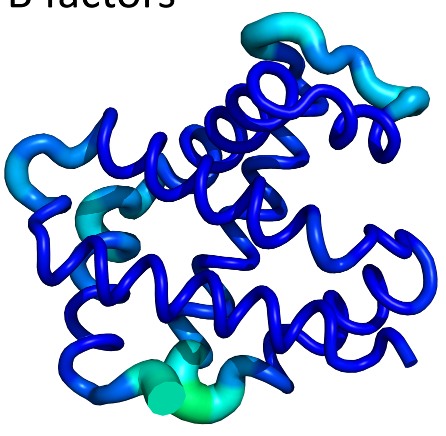
- Results fro structures derived from X-ray crystallography look very similar

C_alphas



NMR
PDB: 2H35

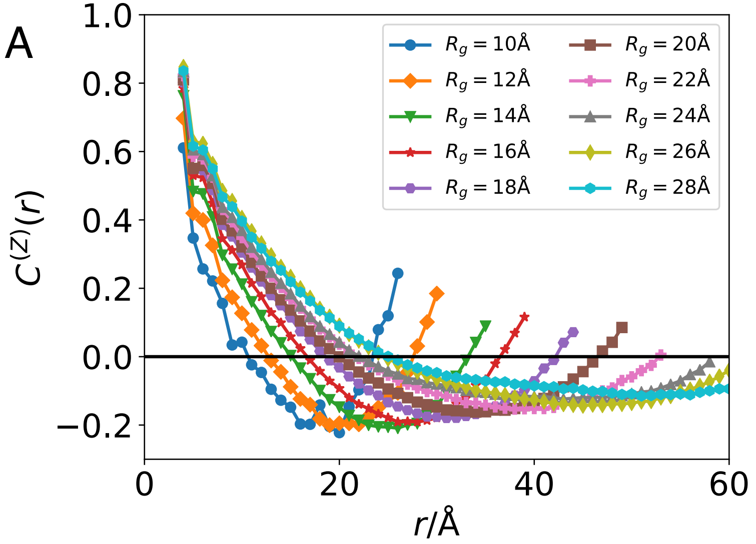
B factors

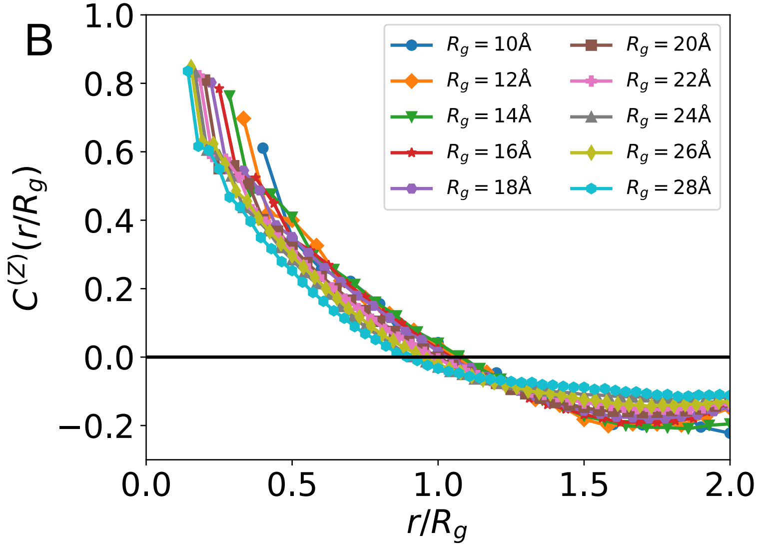


X-ray diffraction
PDB: 2W72

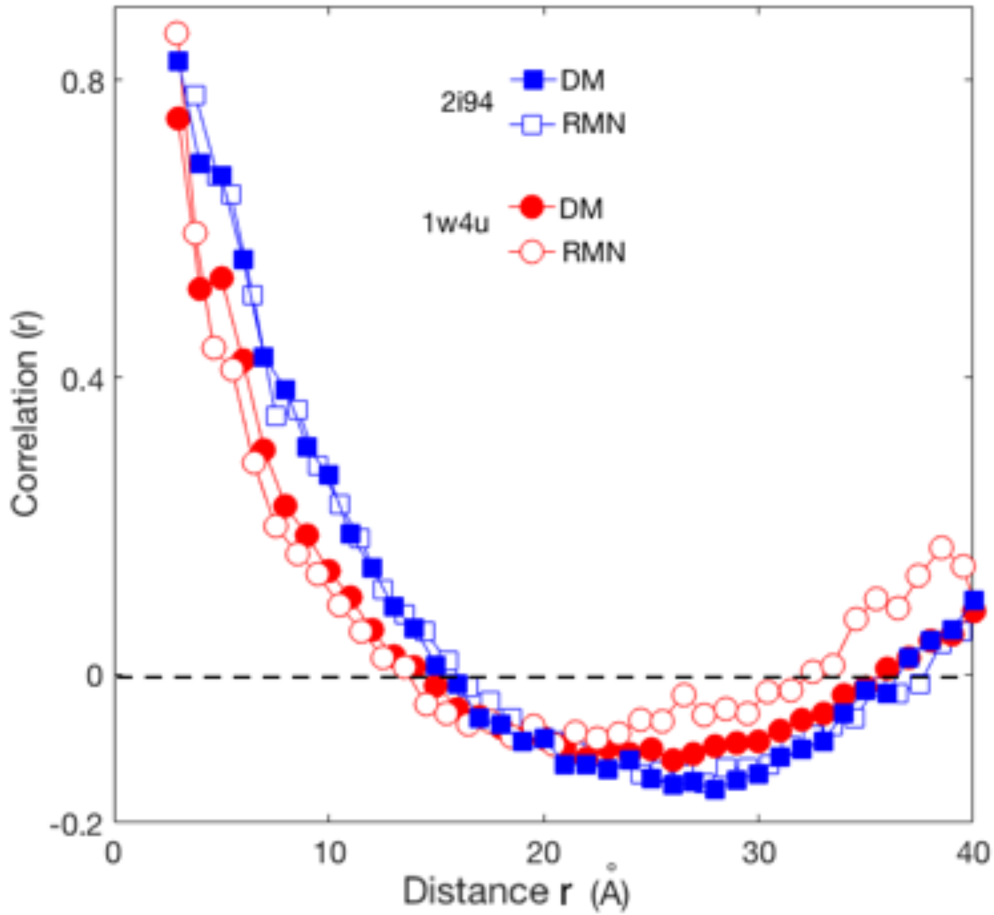
Hemoglobin

Left: Ribbon diagram of the C_alpha set superposed by least squares.
Right:Putty cartoon of B-factor variation on the mean structure (colored from low to high)





- Comparison with molecular dynamics results looks promising



Connected Correlation Functions computed from the PDB structure (RMN) and from C_alpha structures derived from molecular dynamics (MD) (work in progress with IG & EA)

Blah-Blah-logy

- The finite size scaling analysis of proteins shows that the “native state” is critical.

- out of 4000 the most frequently observed are the highly susceptible ones (which has also a preferred shape)

The implications are numerous:

- Different type of sequence-structure predictions
- Different view of allosteric changes
- protein-protein interaction (critical?)
- …

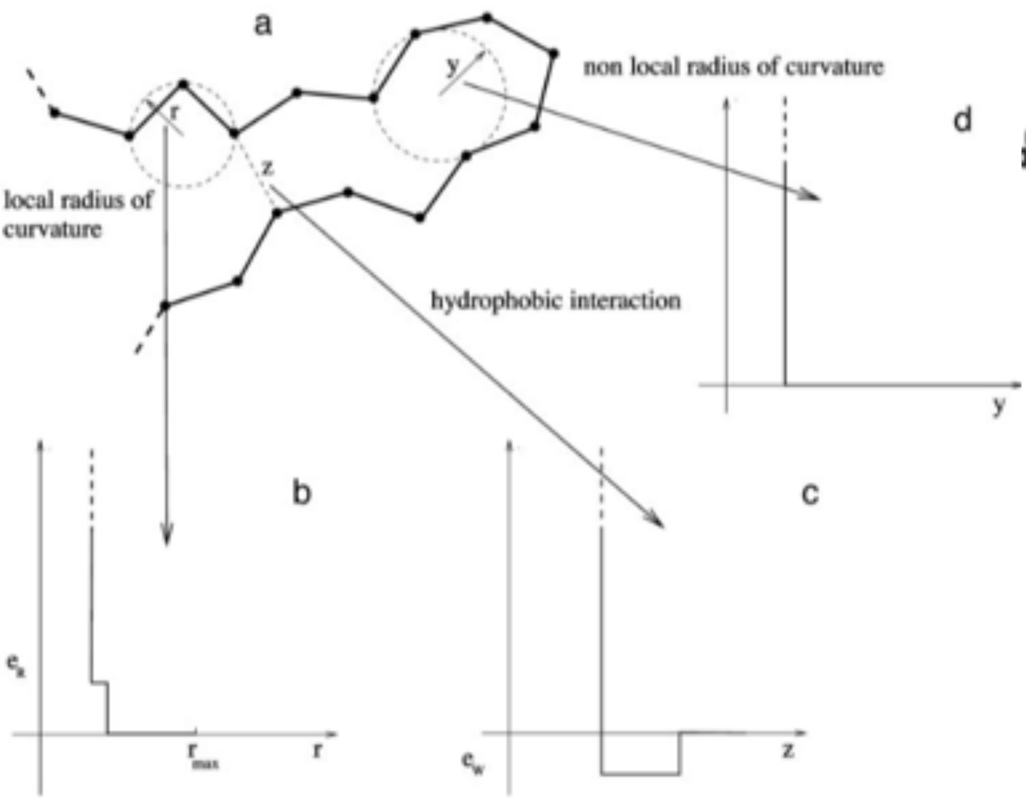
work in progress:

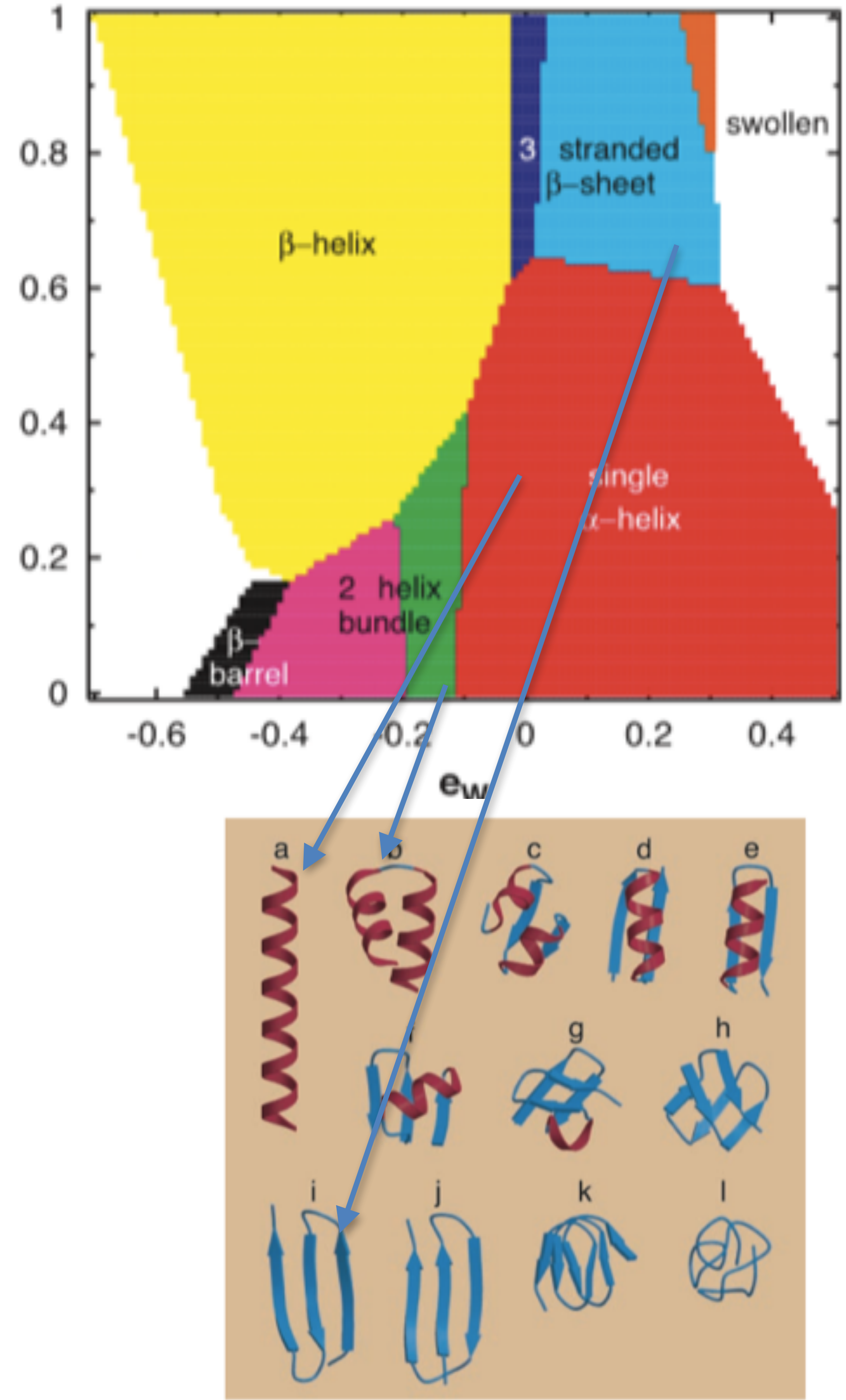
-Analysis conducted for x-ray crystallography B-factors shows similar results

-Molecular dynamics results are pretty consistent too.

-toy model

Hoang (Padova) model





Hoang et al, PNAS (2004) 101 (21) 7960-7964

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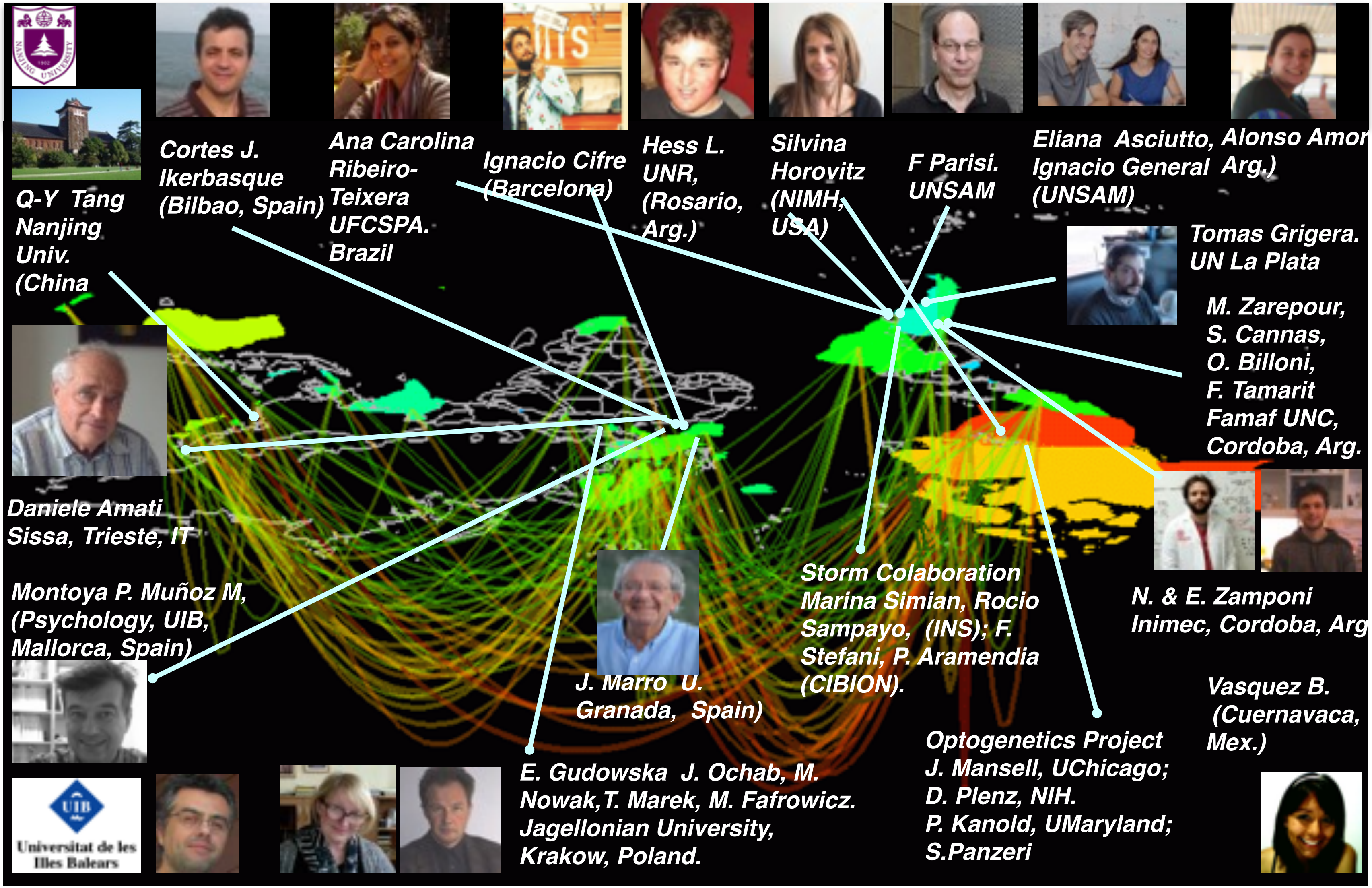
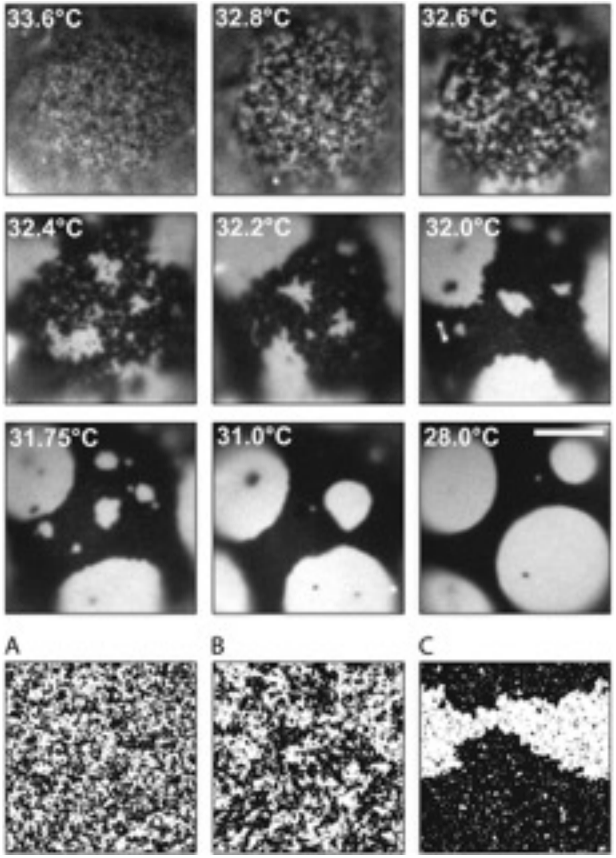
ESCUELA DE CIENCIA Y TECNOLOGÍA

Come visit us!

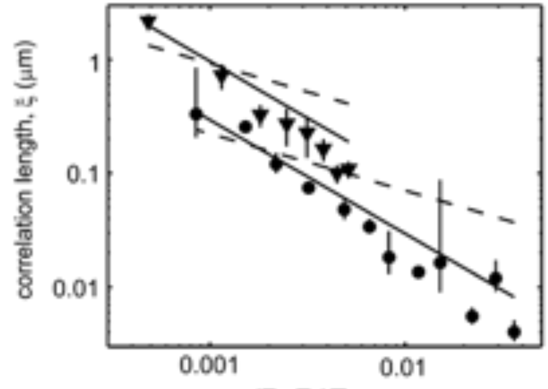
CEMSC^3 -Center for Complex Systems & Brain Sciences
Universidad Nac. de San Martin
Conicet, Argentina

Thanks to all collaborators





Giant unilamellar vesicle passing through a miscibility critical point at T_C 32.5°C. Scale bar is 20 um. The bottom row (A–C) shows Ising model simulations at rescaled temperatures



Correlation length plotted on a log-log scale vs reduced IT-TcI/ Tc. (slope is the critical

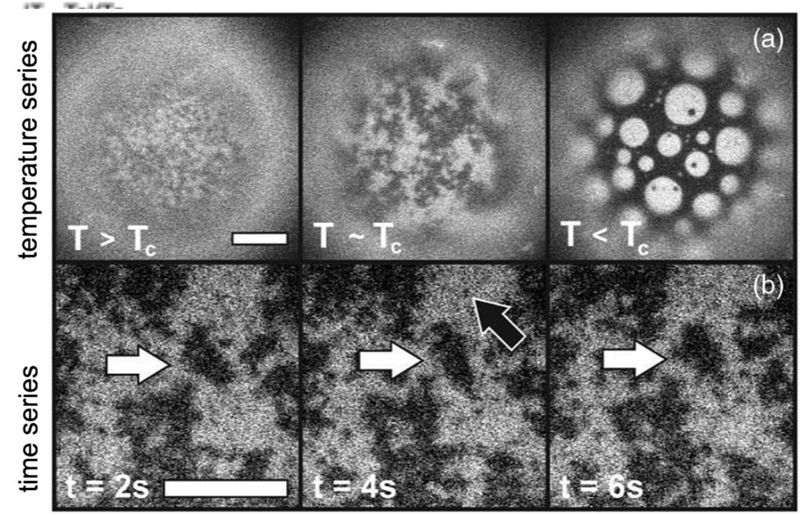


FIG. 1. Fluorescence micrographs of vesicles of diameter 200 μm. (a) As temperature changes from $T > T_c$ ($T = 31.25\,^\circ$C, $T_c \approx 30.9$) to $T \sim T_c$ ($T = 31.0\,^\circ$C), fluctuations in lipid composition grow. Below T_c, at $T = 28\,^\circ$C, domains appear. Scale bar = 10 μm. (b) A movie of composition fluctuations within a vesicle above T_c. Large fluctuations persist for seconds (white arrows), whereas small ones disappear by the next frame (black arrow). Scale bar = 20 μm.

from Honerkamp-Smith et al,

Biophysical Journal 95, 236,(2008)

from Honerkamp-Smith et al, PRL 108,(2012)