NMR ANOMALOUS DIFFUSION MEASUREMENTS TO INVESTIGATE COMPLEX SYSTEMS

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Main Reference: Scientific Reports, 3, 2631 (2013)

- Molecular self-diffusion in heterogeneous porous media can be used to reconstruct statistical properties of the disorder

- ***Diffusion NMR*** is a non-invasive experimental tool to measure ordinary and anomalous diffusion in biological tissues and porous media

- Often diffusion show non-Gaussian anomalies, i.e. the diffusion coefficient D depends on time in a certain t-window.

AIM

Detect system structural complexity and disorder transitions through the anomalies of molecular self-diffusion found by NMR

Saxton M.J., *Biophys. J. 92 (2007)*
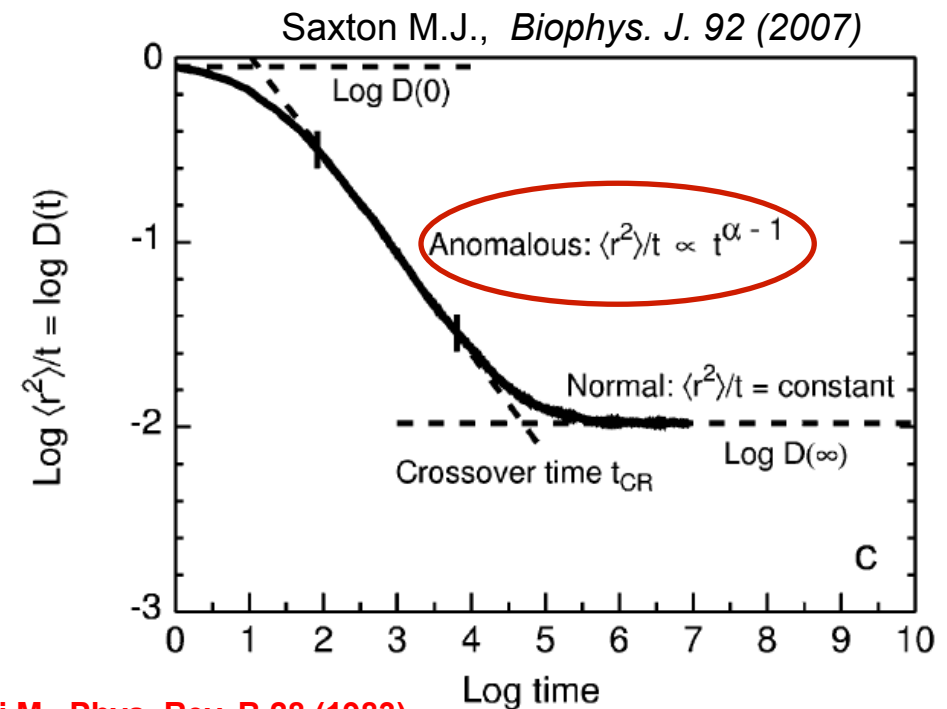
Steinhardt P.J., Nelson D.R., Ronchetti M., Phys. Rev. B 28 (1983)

NMR for dummies

NMR is non-invasive experimental tool to provide a 3d measure of nuclear magnetic moments (e.g. H^+) density in biological tissues and materials and related relaxation times of energy populations
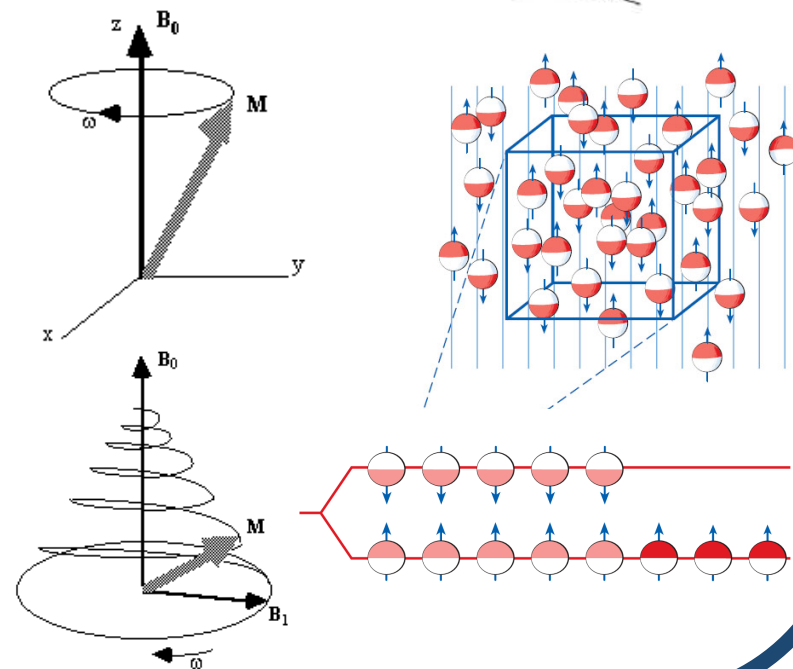
MAGNETIC DISCUSSION

These quantities can be used both for spectroscopy and imaging

Particular NMR experimental protocols can implemented to measure H^+ ions diffusion:
Pulse Gradient Spin Echo (PSGE) sequence

Main ideas of anomalous diffusion MRI

• Study of water diffusion in heterogeneous materials has great importance in many interdisciplinary fields (e.g. biology, medicine *in vivo,* brain science)

• NMR + generalized diffusion theory, e.g. Continuous Time Random Walk (CTRW), provides a natural, powerful and non-invasive tool to study structure in biological tissues and disordered materials

• dNMR permits both to characterize the spatial features of obstacles studying sub-diffusion effects

[For chemio-physical properties detected through pseudo-superdiffusion induced by gradients of magnetic susceptibility – See M Palombo talk in "Brain" satellite meeting]

M Palombo, AG, S De Santis, C Cametti, G Ruocco, S Capuani, J. of Chem. Phys., **135**, 034504 (2011)
M Palombo, AG, S De Santis, S Capuani, J. of Mag. Res., **216**, 28 (2012).

Diffusion Magnetic Resonance Imaging (dMRI)

One can encode spatial information of different points in the NMR signal through static and uniform gradients **G** of the polarizing field:
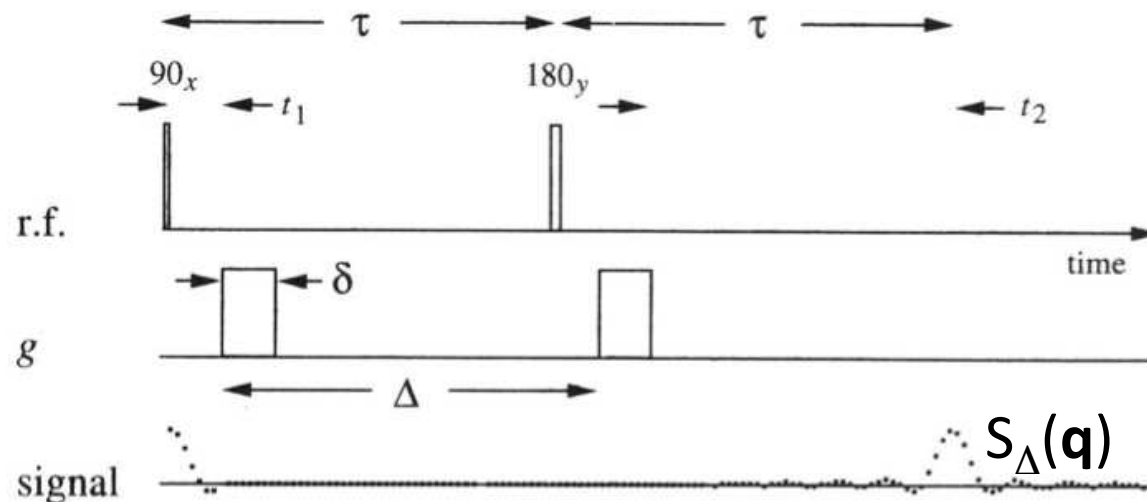After a time t the phase of the spins depend on their position *r.*

In principle we can write

$$\vec{B}(\vec{r}) = \hat{z}B_0 + \vec{G}\cdot\vec{r} \Rightarrow \omega(\vec{r}) = \gamma(B_0 + \vec{G}\cdot\vec{r})$$

Larmor frequency depends on the position *r*: with appropriate experimental protocols one can use phase differences to detect displacements and then study random motions.

Pulse Gradient Spin Echo (PSGE) sequence

- Let us suppose that the spin at $t=0$ is at **r** and at $t=\Delta$ is at **r'**.
- If δ is small, the gradient after the first radiofrequency pulse gives a phase shift $\gamma\delta\mathbf{g}\cdot\mathbf{r}$ at **r.**
- The gradient after the second radiofrequency which reverse the spins gives a phase shift $-\gamma\delta\mathbf{g}\cdot\mathbf{r'}$ at **r'**.
- The net phase coefficient is therefore $\exp[i\gamma\delta\mathbf{g}\cdot(\mathbf{r}-\mathbf{r'})]$

Therefore, neglecting R_2, the attenuation of the signal due to diffusion is

$$S_\Delta(\vec{q}) = \int d^3R \cdot p(\vec{R}, \Delta) \exp(i\vec{q} \cdot \vec{R})$$

where $\vec{R} = \vec{r} - \vec{r}'$ and $\vec{q} = \delta\gamma\vec{g}$ and

$$p(\vec{R}, \Delta) = \text{propagator of the diffusion in time } \Delta$$

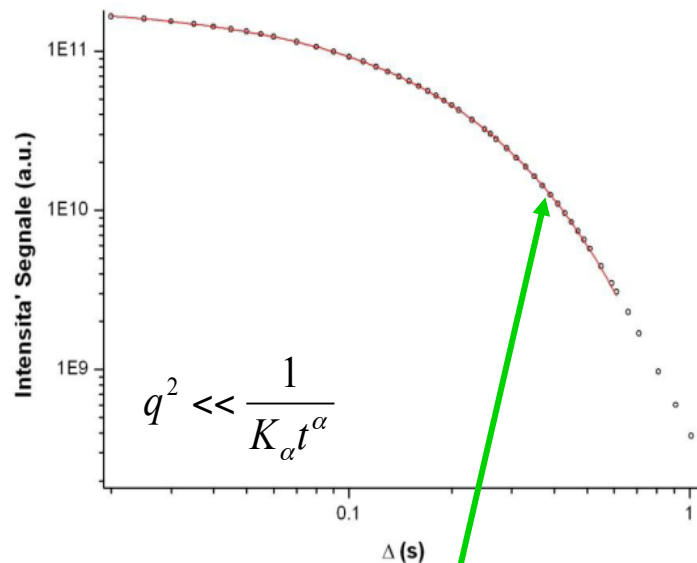E.g. in case of ordinary Gaussian diffusion in that time window

$$S_\Delta(\vec{q}) = \int d^3R \cdot p(\vec{R}, \Delta) \exp(i\vec{q} \cdot \vec{R}) = \exp(-D\Delta q^2)$$

e.g. DTI= Diffusion Tensor Imaging

CTRW: how to measure α by NMR technique

α: Δ varying PGSE

$$q^2 \ll \frac{1}{K_\alpha t^\alpha}$$

Intensita' Segnale (a.u.)

Δ (s)

$$S(\Delta) = S(0) \exp\left(- K_\alpha q^2 \Delta^\alpha\right)$$

TR/TE = 3000/8 ms
δ = 2ms;
For γ :
Δ = 80 ms; g = (24 ÷ 960) mT/m
For α :
Δ = (10 ÷ 1300) ms; g = 120 mT/m

Ordinary materials: CLT

Diffusion in disordered systems with <u>characteristic</u> constraining length scale
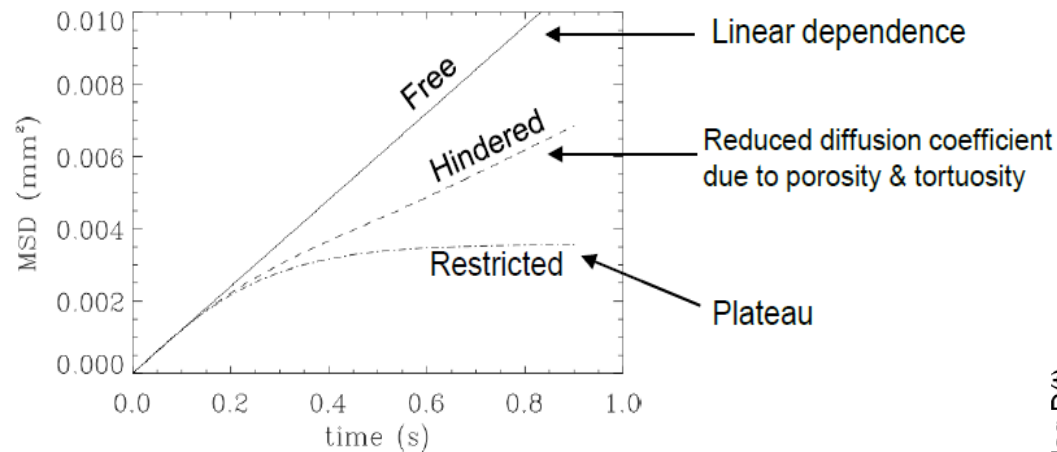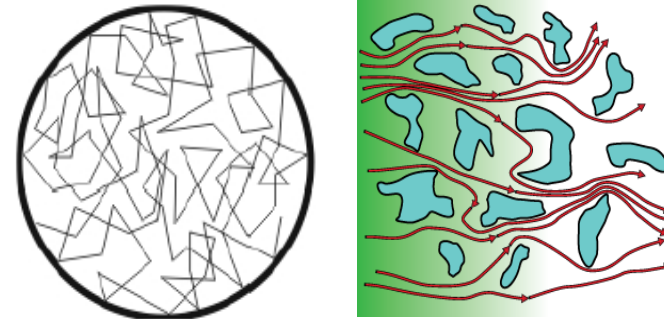
Typical in most of disordered systems
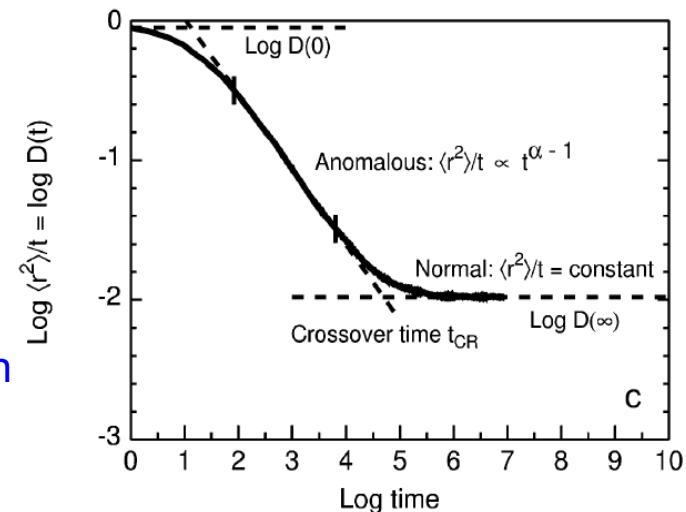
- At small t free ordinary diffusion: p(R,t) Gaussian
- At large t hindered ordinary diffusion (caging effects due to heterogeneities are averaged out): p(R,t) Gaussian
- At intermediate t effective anomalous sub-diffusion (sensibility to heterogeneities)
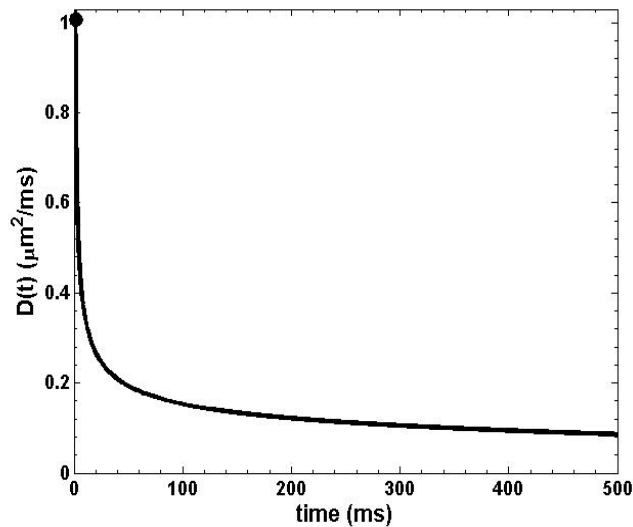
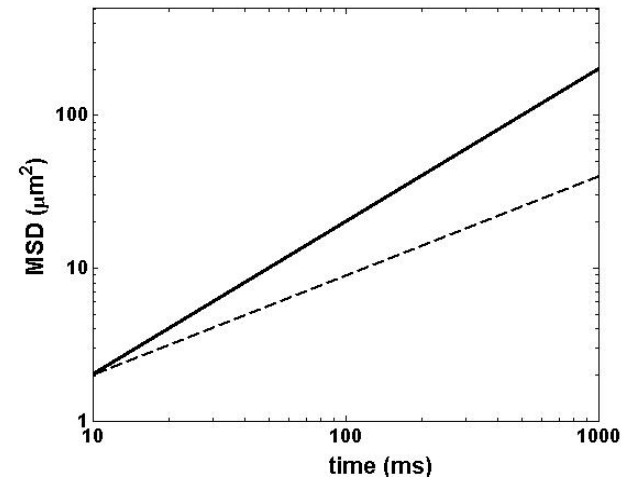Bouchaud J.P., Georges A*., Phys. Rep. **195** (1990)*

Violation of Central Limit Theorem

1) The *value* of transport coefficients are not constant: no characteristic scale

2) The very *laws* of Brownian motion are modified in various ways: memory effects and time correlations, broad resting time pdf, etc.: **e.g. CTRW**
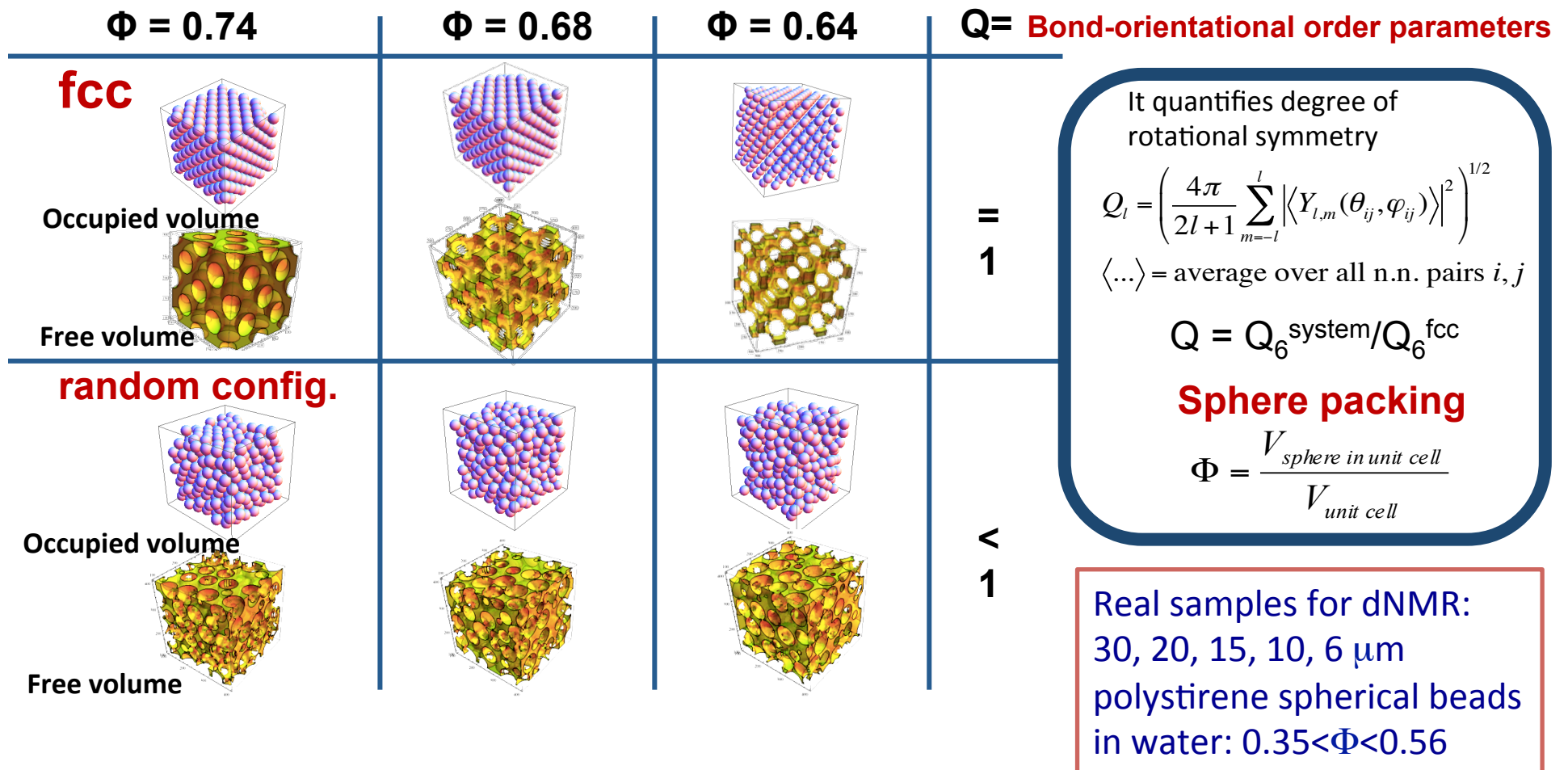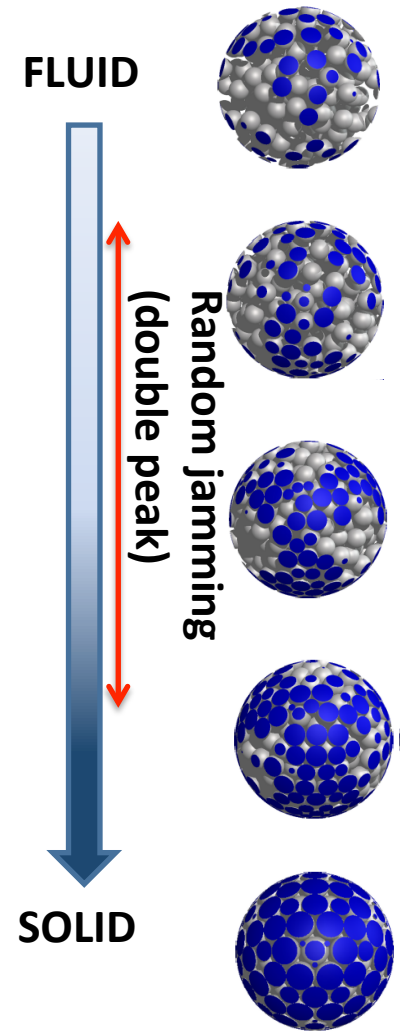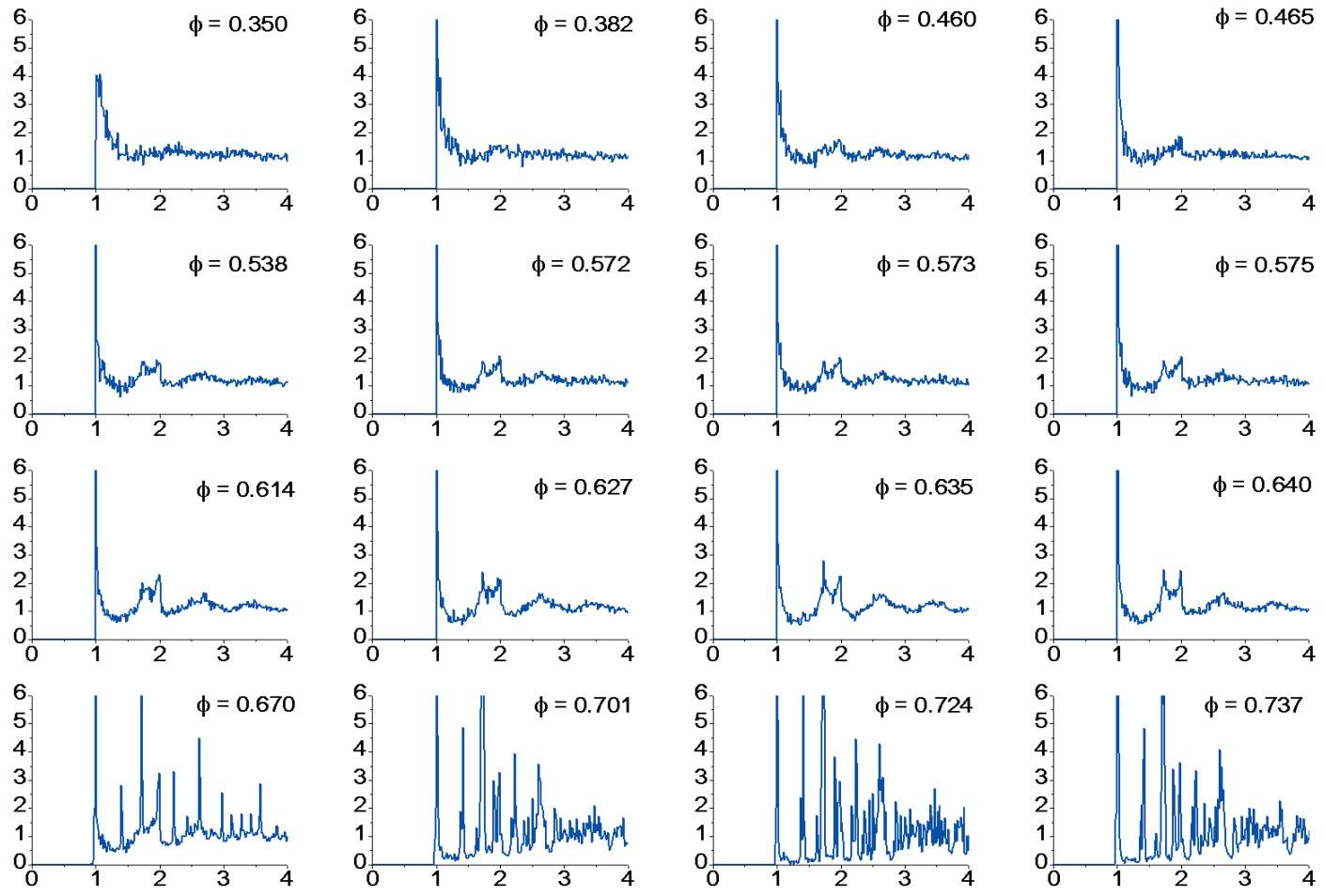
$$D = D(t)$$

$$MSD \propto t^{\alpha}, \alpha < 1$$

Bouchaud J.P., Georges A.*, Phys. Rep. **195** (1990)*

Porous media arising from regular and disordered sphere packing

$\Phi = 0.74$	$\Phi = 0.68$	$\Phi = 0.64$	Q= **Bond-orientational order parameters**
fcc Occupied volume Free volume			= 1
random config. Occupied volume Free volume			< 1

It quantifies degree of rotational symmetry

$$Q_l = \left(\frac{4\pi}{2l+1} \sum_{m=-l}^{l} \left| \langle Y_{l,m}(\theta_{ij}, \varphi_{ij}) \rangle \right|^2 \right)^{1/2}$$

$\langle ... \rangle$ = average over all n.n. pairs i, j

$$Q = Q_6^{system}/Q_6^{fcc}$$

Sphere packing

$$\Phi = \frac{V_{sphere\ in\ unit\ cell}}{V_{unit\ cell}}$$

Real samples for dNMR: 30, 20, 15, 10, 6 μm polystirene spherical beads in water: $0.35 < \Phi < 0.56$

From *random fluid* to *disordered poly-crystal* through *jamming transition*

Inset equation:
$$n_c = n_c^0 \frac{1 + m\phi^4}{1 + n\phi^4}$$

Inset labels: n_c, ϕ, RPT, SPT

Curve labels (right axis): fcc, 0.737, 0.670, 0.640, 0.572, 0.460, 0.350
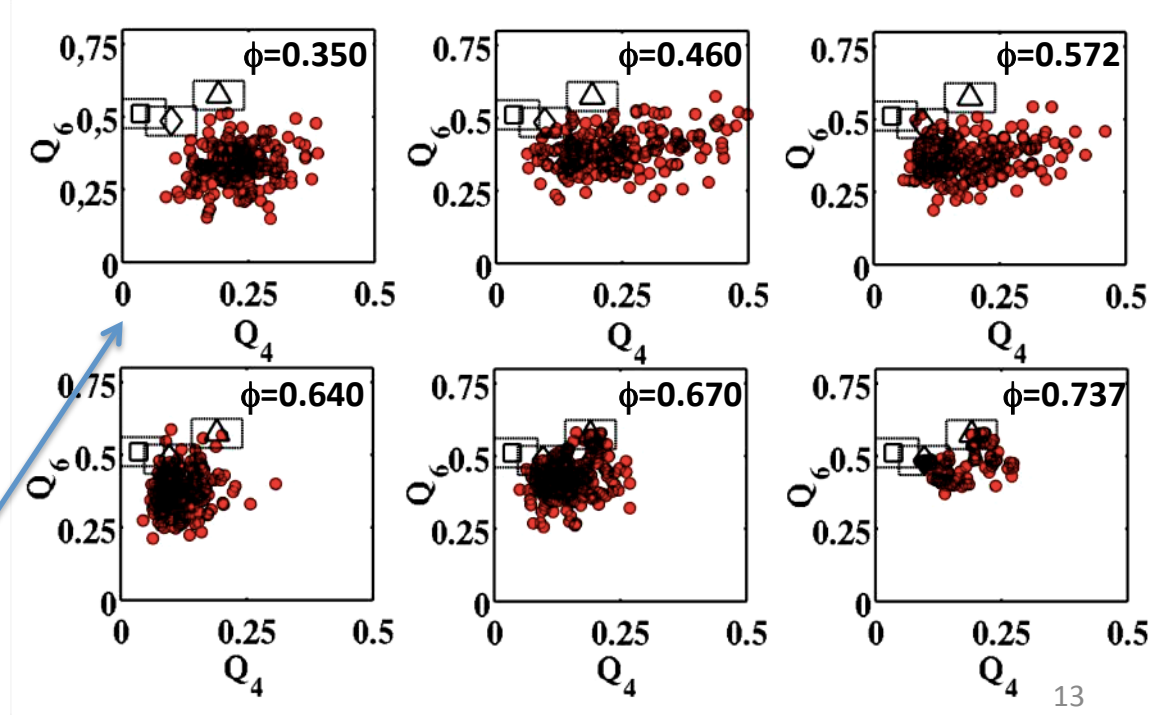
Axis labels: $n_t(r)$, r/d
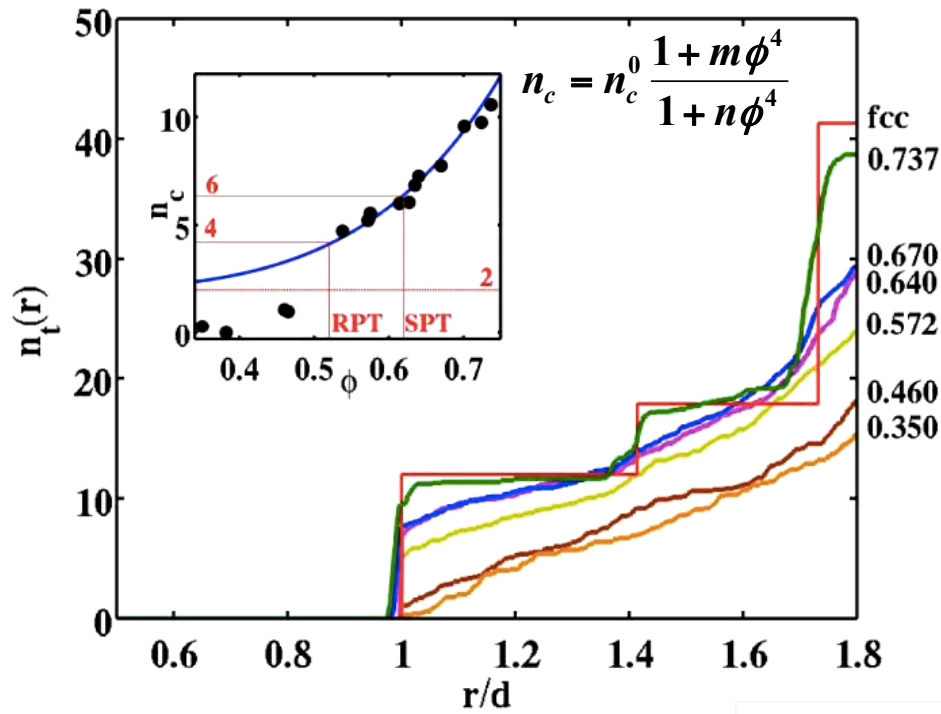
Two structural transitions:

1

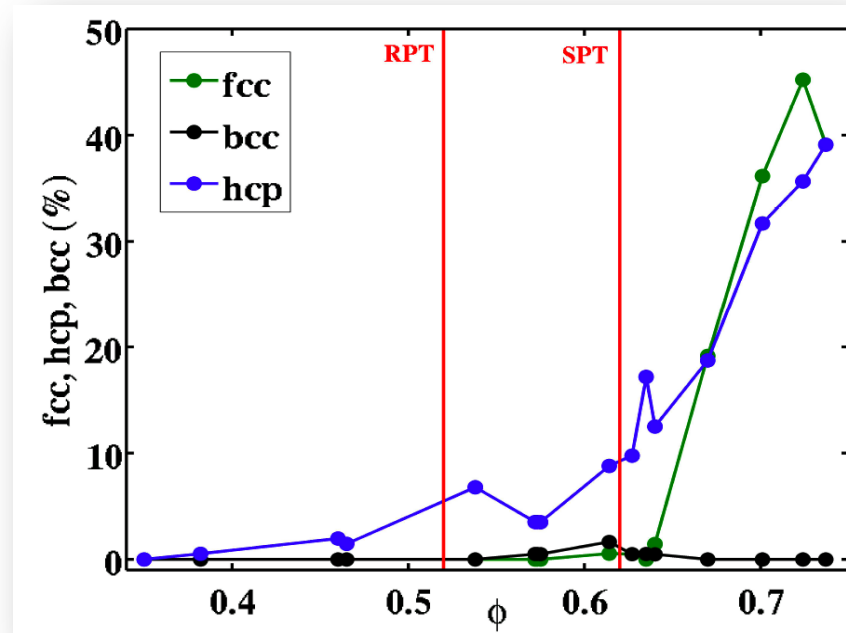*Rigid but unstressed structure*
(RPT at $\phi = 0.52$)

2

Stressed structure
(abrupt transition SPT at $\phi = 0.62$)

Densest packings exhibit a **poly-crystal structure** with grains mainly ordered on **fcc (△)** and **hcp (◇)** structures

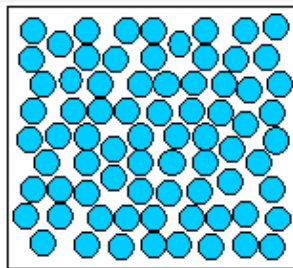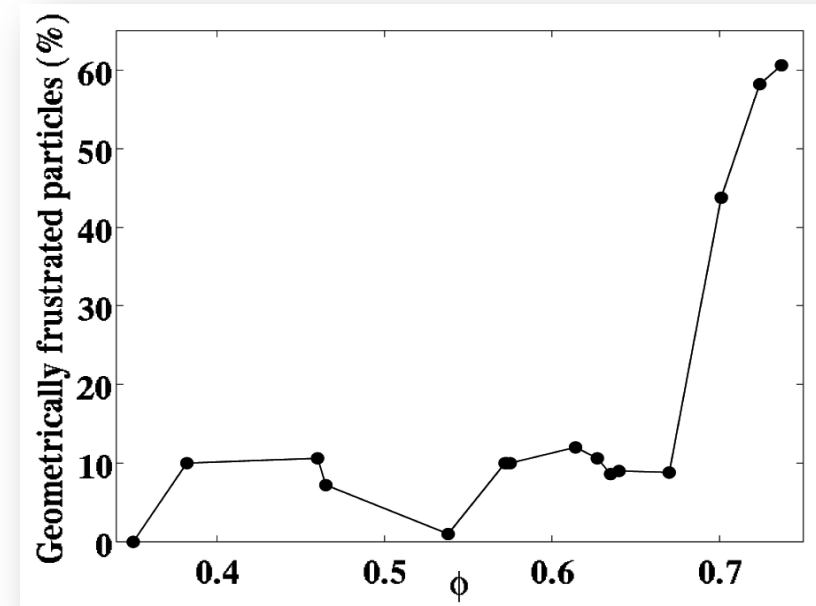Good detector of SPT transition

$\phi = 0.350$, $\phi = 0.460$, $\phi = 0.572$, $\phi = 0.640$, $\phi = 0.670$, $\phi = 0.737$

Axis labels: Q_6, Q_4

Fraction of configurations close to crystal

Fraction of particles with local $\Phi_i > \Phi_{fcc}$

RPT   SPT

fcc
bcc
hcp

fcc, hcp, bcc (%)

ϕ

Geometrically frustrated particles (%)
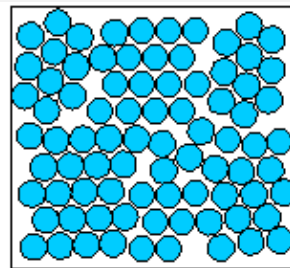
ϕ

Amorphous solid
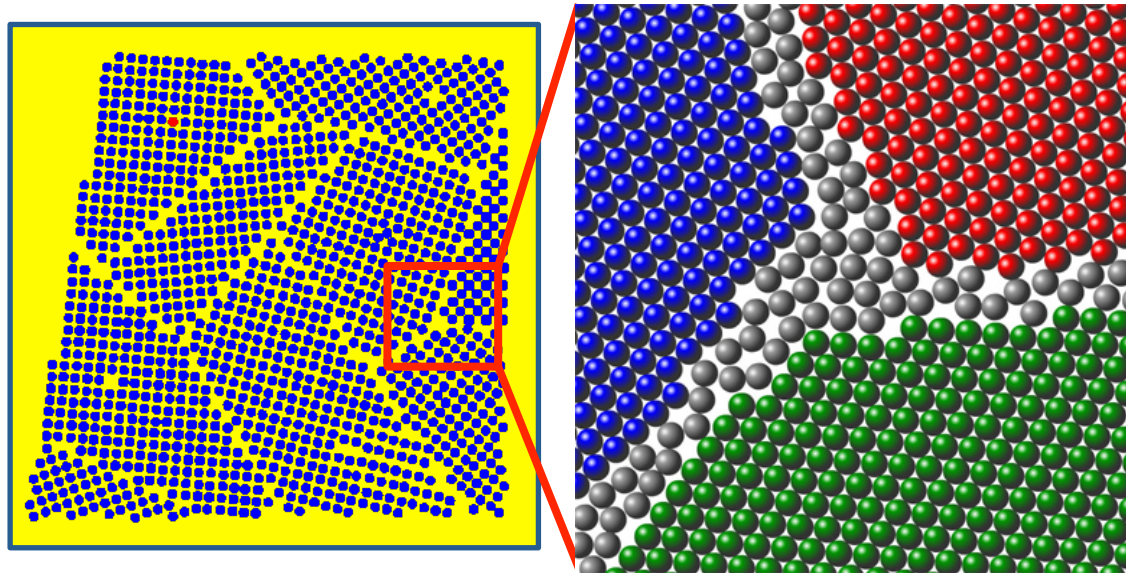
Not periodic.

Polycrystal

Periodic across
each grain.

Densest packings exhibit
geometrically frustrated
grains mainly ordered on
fcc and **hcp** structures

Densest disordered configurations: frustrated grains locally arranged in impossible ordered configurations (e.g. icosahedral) creates large heterogeneities.

Wide distribution of voids characteristic length scales which reflects disorder properties: multi-scale hindering

Wide distribution of voids
MAITI M.; LAKSHMINARAYANAN A.; SASTRY S.. *The European Physical Journal E*, 2013, 36.1: 1-13.

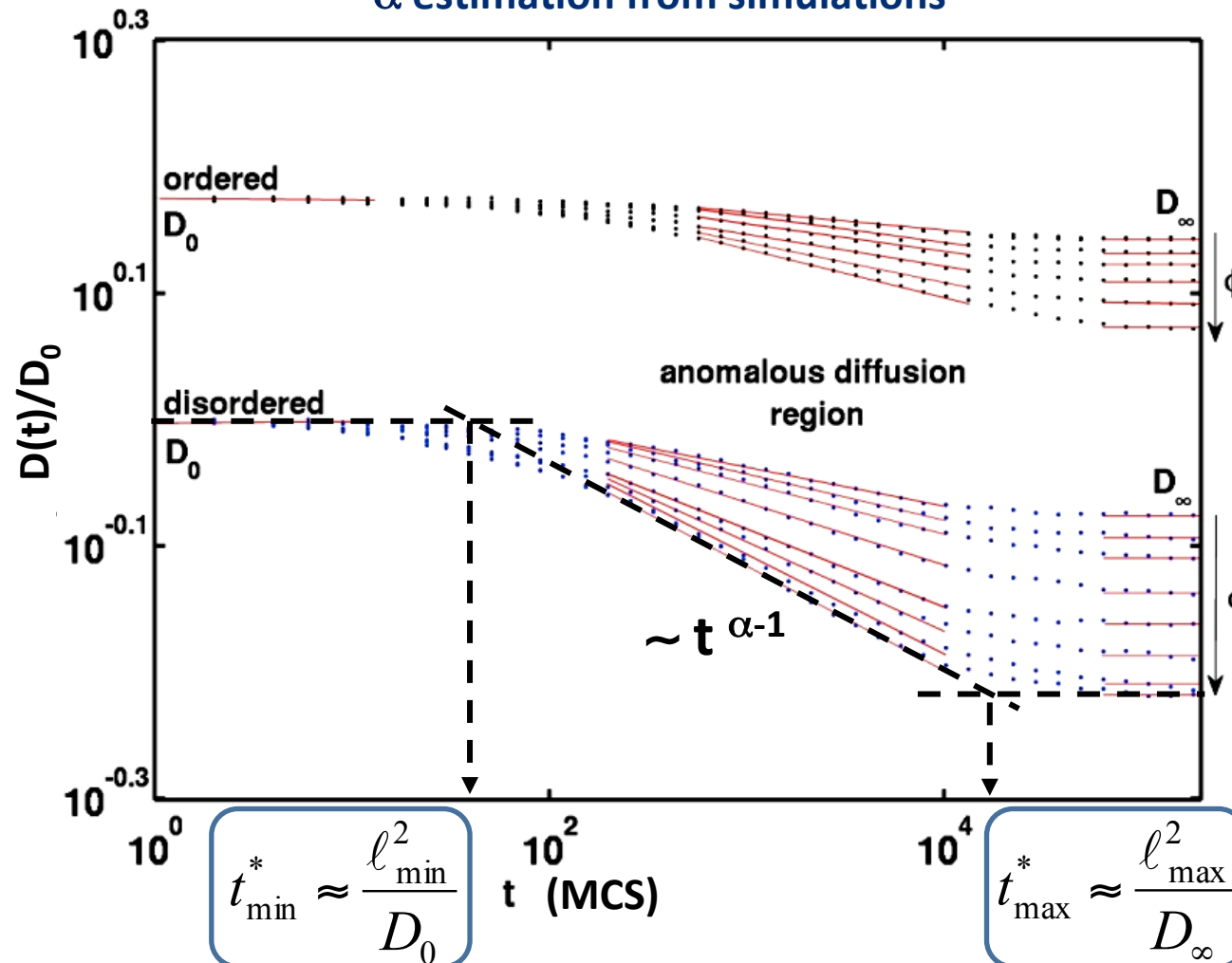→ **Broad distribution of diffusing molecules waiting times** → **Sub-diffusion $\alpha < 1$**
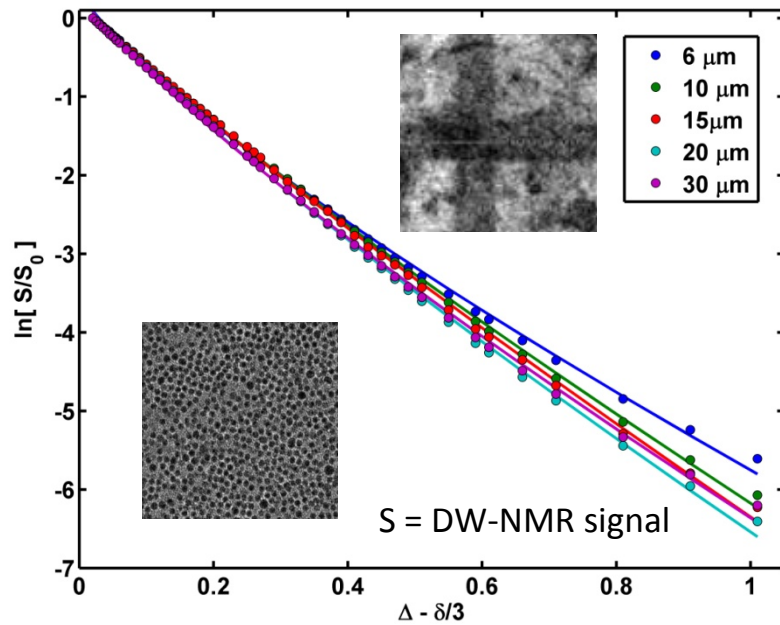
L. Gránásy et al. *Nature Materials* 3, 645-650 (2004)

Molecular diffusion in the hindered regime can describe these properties and monitor structural transitions
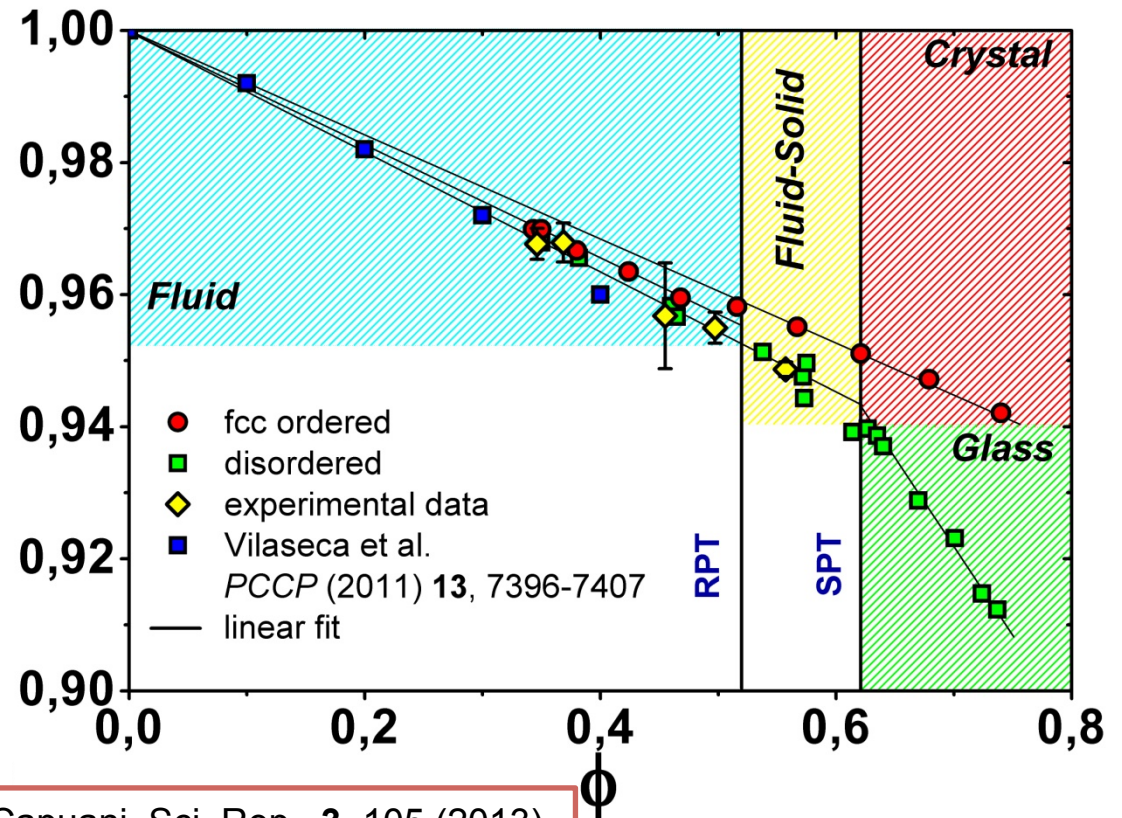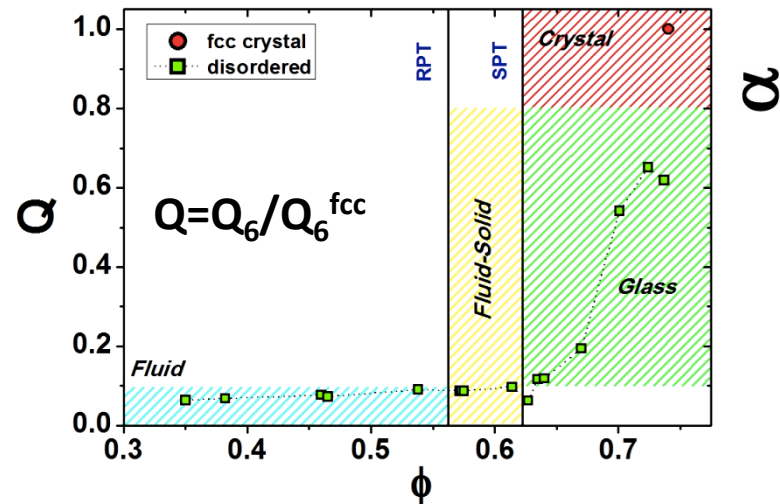

α estimation from simulations

From geometrical structure characterization to anomalous diffusion properties:

comparison of Monte Carlo simulation results to dNMR experimental data

S = DW-NMR signal

$Q=Q_6/Q_6^{fcc}$

M Palombo, AG, VDP Servedio, G Ruocco, S Capuani, Sci. Rep., **3**, 105 (2013)

- Our computational data indicate that α, which quantifies hierarchical caging effects on diffusion process, is affected by both the density (Φ) and the spatial distribution (Q) of obstacles:

$$\alpha = \alpha(Q, \Phi)$$

- α value quantifies global structural complexity much better than tortuosity parameter $O_D = \Phi_D/\Phi_0$. It enables a classification of different kinds of disorder and it allows to monitor structural transitions.

- We demonstrated that α can be measured by non invasive and non destructives diffusion NMR techniques.

- Our NMR experimental results, obtained in packed polystyrene micro-sphere systems, fully confirm simulation results.

- The present work suggests that α may be used to quantify unresolved effects due to heterogeneities and disorder in soft materials and living tissues.