From inelastic X-ray scattering to neurosciences

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ISTITUTO ITALIANO DI TECNOLOGIA
CENTER FOR LIFE NANO SCIENCE

SAPIENZA
UNIVERSITÀ DI ROMA

Summary

1980-2006 **Physics of Soft Matter, Liquids and Glasses**

GLAS INFM Soft INFM Complex Dynamics in Structured Systems

2007-2014 **University Management**
(Physics Dept.: Director, Sapienza: Research Policy Vice Rector)

SAPIENZA
UNIVERSITÀ DI ROMA

2015-..... **From Physics to Neuroscience**

ISTITUTO ITALIANO DI TECNOLOGIA
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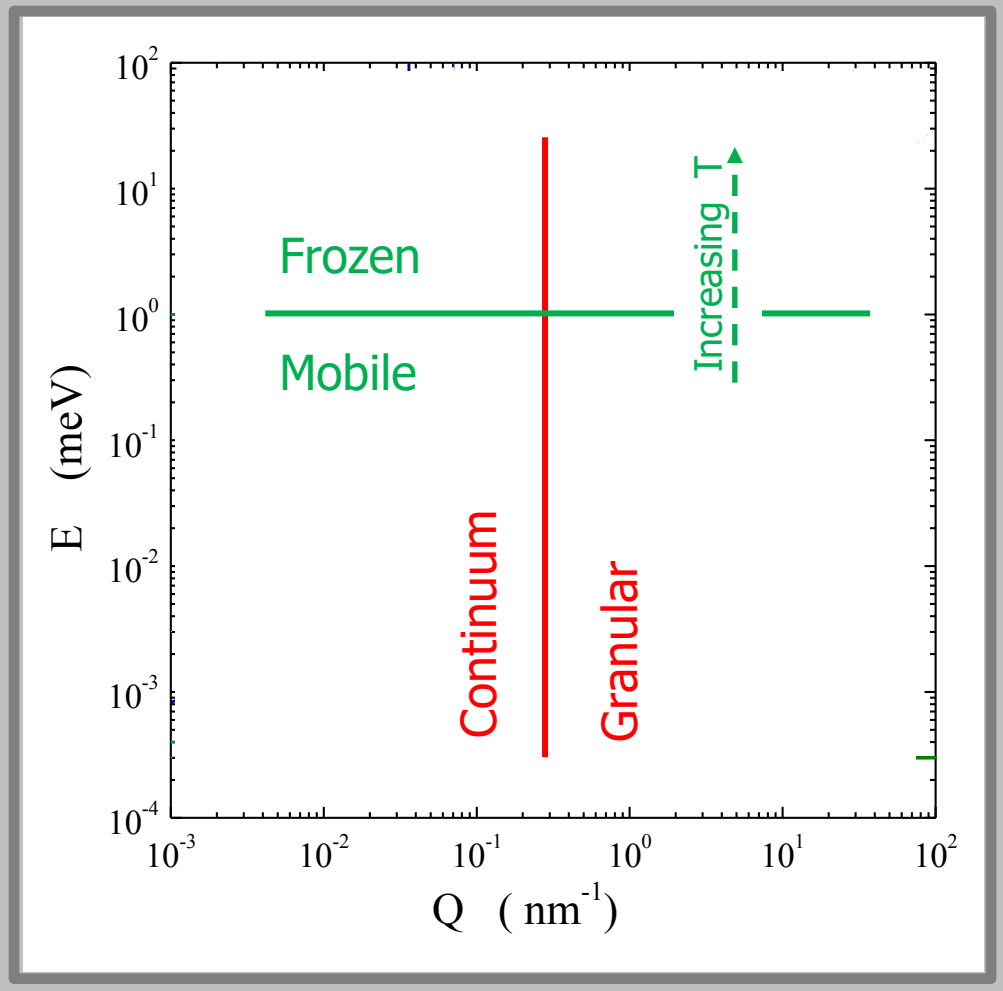
Summary

1. High frequency excitation in glasses: the Q-E region
2. Diagnosis of Tumors via animal based biosensor
3. New dimension in microscopy: imaging mechanical properties
4. Diagnosis of Neurodegenerative Diseases (AD, PD, AMD, ALS, …) via newly developed HR/LWD imaging systems.

High frequency dynamics in disordered systems

Length-scale λ

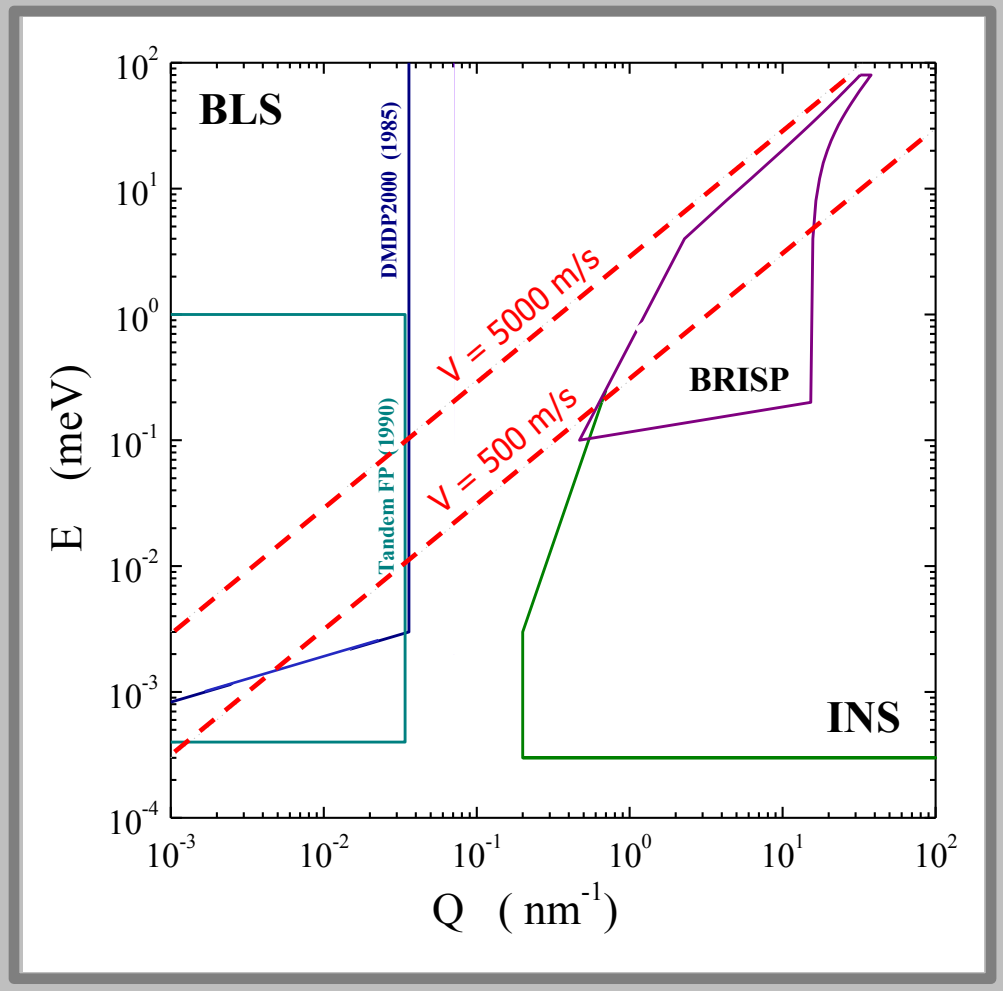
Time-scale τ



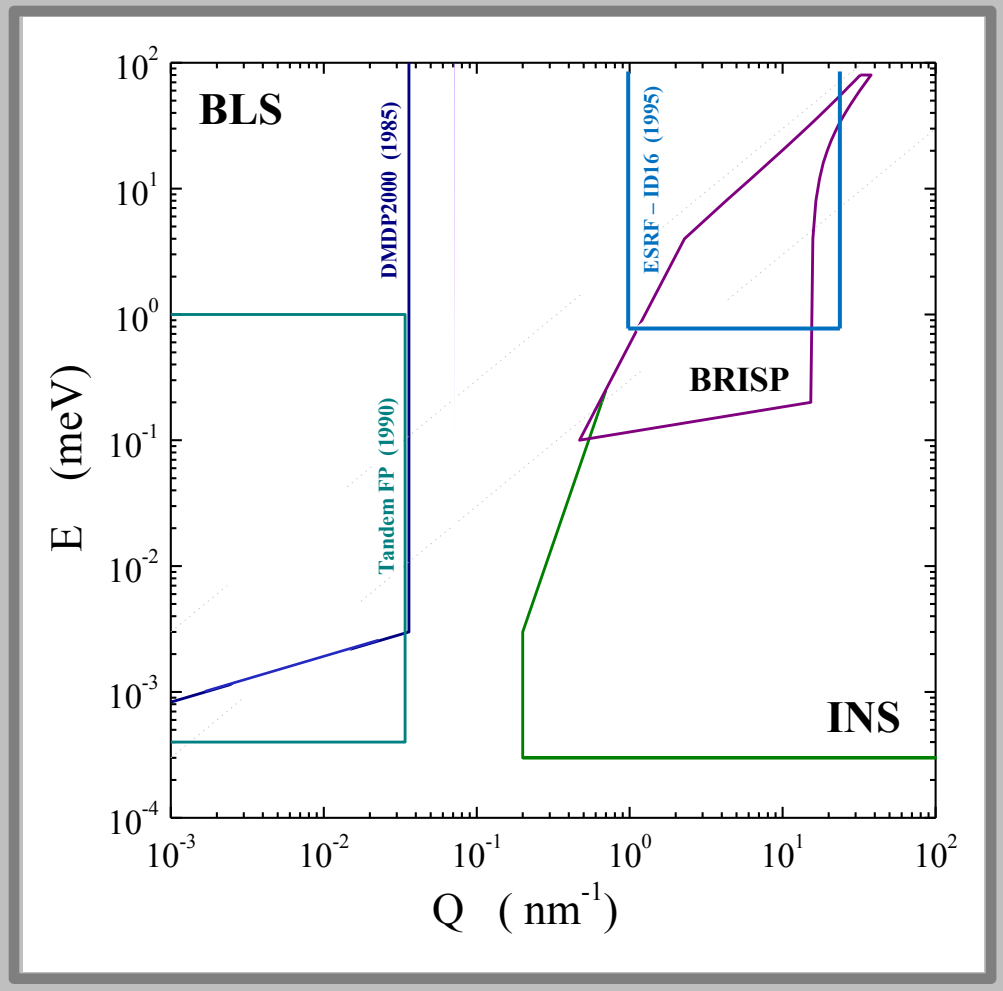
$Q = 2\pi\ \lambda^{-1}$

$E = h\nu = h\tau^{-1}$

High frequency dynamics in disordered systems



High frequency dynamics in disordered systems



1 – Existence of excitations in glasses

SiO_2

SCIENCE • VOL. 280 • 5 JUNE 1998 • www.sciencemag.org

Dynamics of Glasses and Glass-Forming Liquids Studied by Inelastic X-ray Scattering

Francesco Sette,* Michael H. Krisch, Claudio Masciovecchio, Giancarlo Ruocco, Giulio Monaco

VOLUME 76, NUMBER 18 PHYSICAL REVIEW LETTERS 29 APRIL 1996

Observation of Large Momentum Phononlike Modes in Glasses

C. Masciovecchio,[1] G. Ruocco,[2] F. Sette,[1] M. Krisch,[1] R. Verbeni,[1] U. Bergmann,[1] and M. Soltwisch[3]
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(Received 19 December 1995)

PRL 96, 135501 (2006) PHYSICAL REVIEW LETTERS week ending 7 APRIL 2006

High-Frequency Dynamics in Metallic Glasses

T. Scopigno,[1] J.-B. Suck,[2] R. Angelini,[1] F. Albergamo,[3] and G. Ruocco[1]
[1]INFM CRS-SOFT and Dipartimento di Fisica, Università di Roma "La Sapienza", I-00185, Roma, Italy
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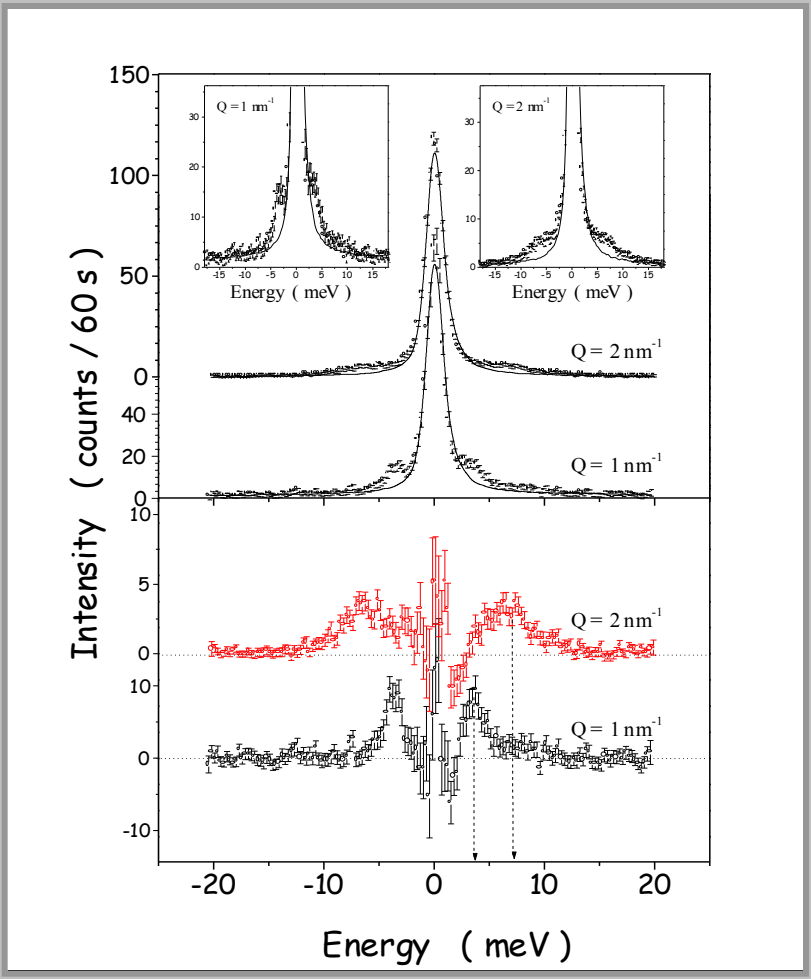
(Received 25 December 2005; published 5 April 2006)



1 – Existence of propagating excitations in glasses (dispersion relation)

VOLUME 92, NUMBER 2 PHYSICAL REVIEW LETTERS week ending 16 JANUARY 2004

High Frequency Dynamics in a Monatomic Glass

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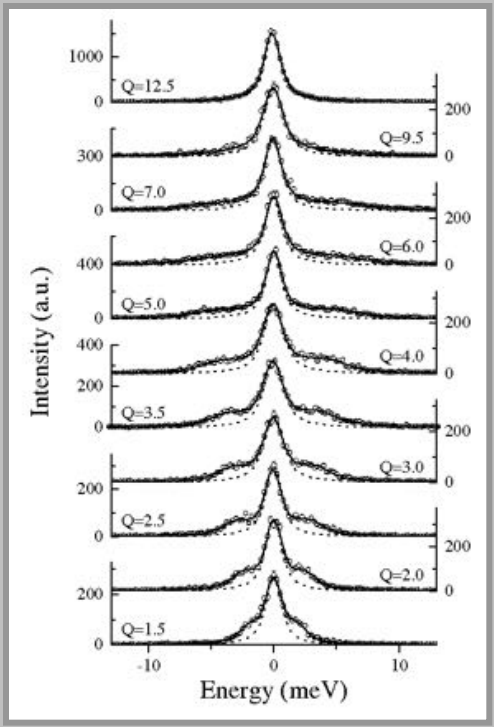
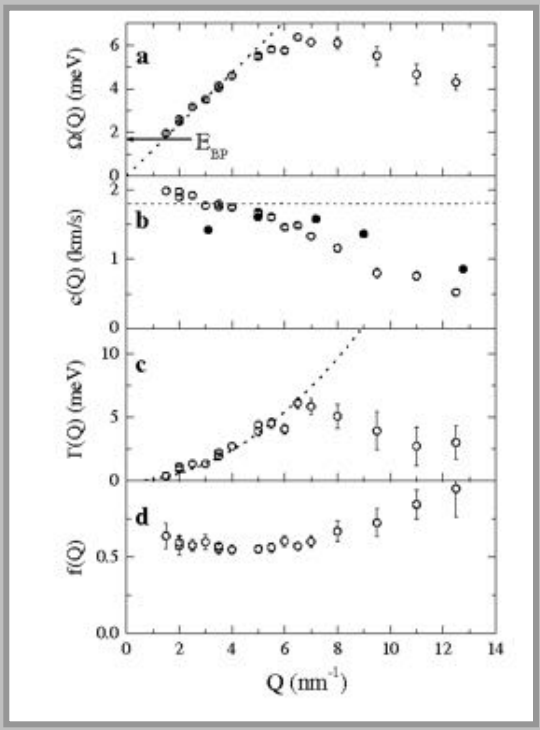
F. Bossard and S. N. Yannopoulos
Foundation for Research and Technology–Hellas, Institute of Chemical Engineering and High-Temperature Chemical Processes, FORTH-ICE/HT, P.O. Box 1414, GR-265 00 Patras, Greece
(Received 26 September 2003; published 16 January 2004)

Selenium





1 – Existence of propagating excitations in glasses (crystal-like dispersion)

PRL 96, 135501 (2006) PHYSICAL REVIEW LETTERS week ending 7 APRIL 2006

High-Frequency Dynamics in Metallic Glasses

T. Scopigno,[1] J.-B. Suck,[2] R. Angelini,[1] F. Albergamo,[3] and G. Ruocco[1]
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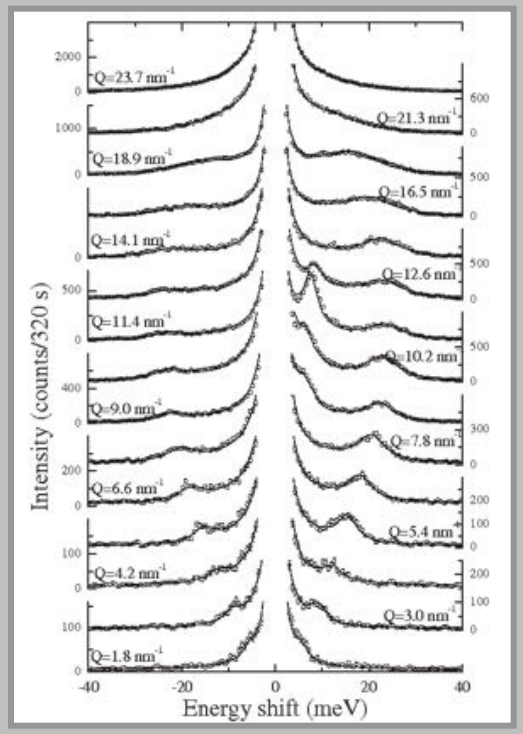
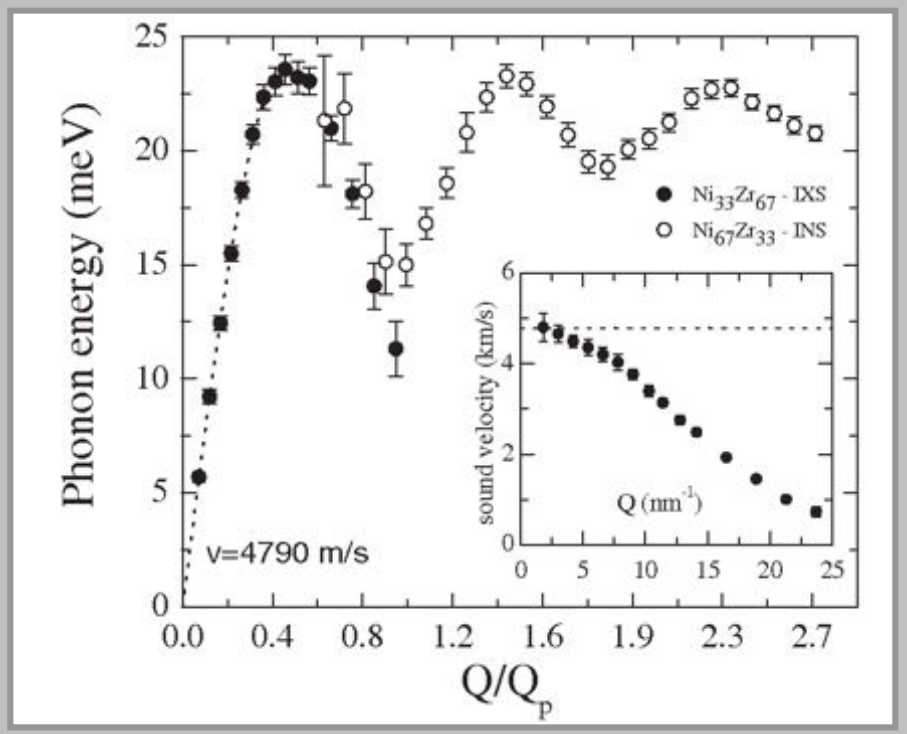
(Received 25 December 2005; published 5 April 2006)

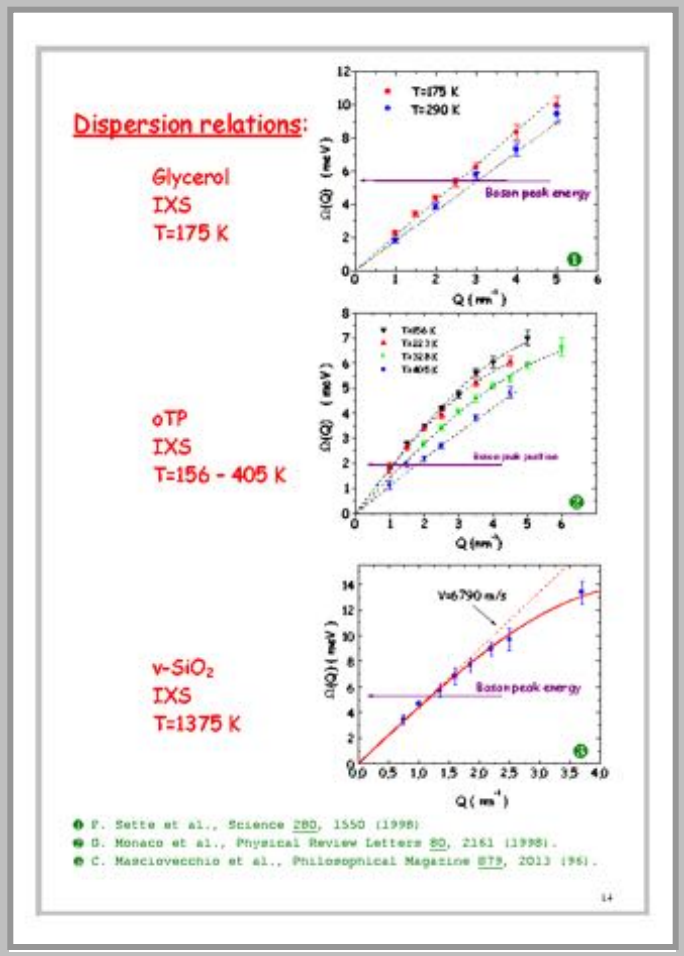
Metallic Glass

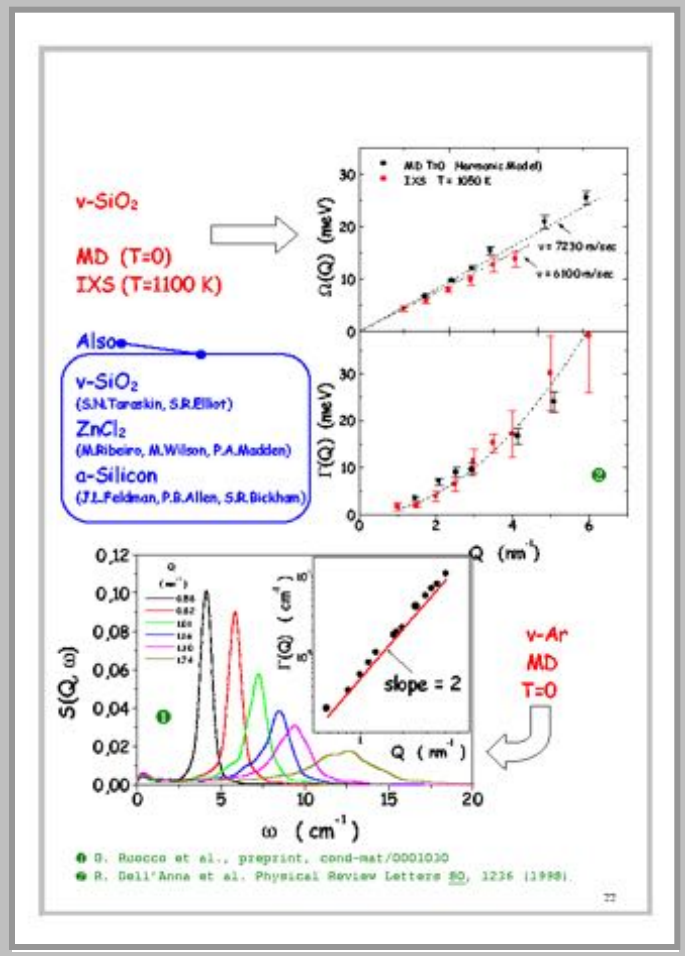
(NiZr)





2 – Existence of propagating excitations at energy well above the Boson Peak Energy





3 – Solid like excitations: Umklap processes

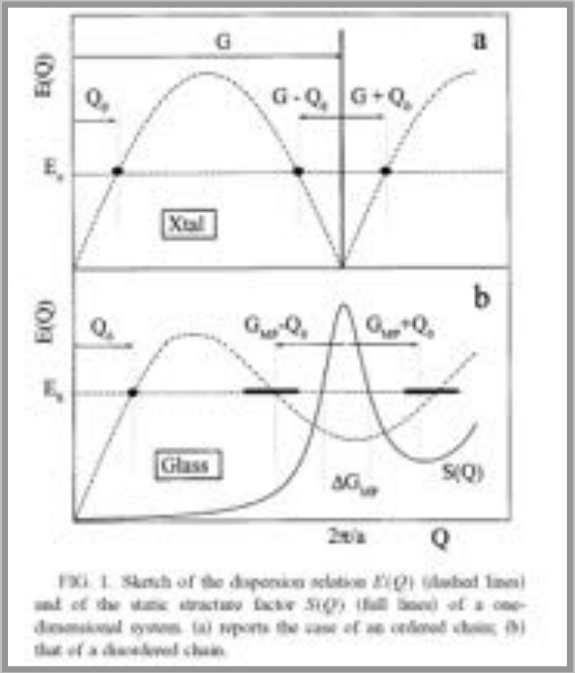


FIG. 1. Sketch of the dispersion relation $E(Q)$ (dashed lines) and of the static structure factor $S(Q)$ (full lines) of a one-dimensional system. (a) reports the case of an ordered chain; (b) that of a disordered chain.

PHYSICAL REVIEW B, VOLUME 64, 012301

Observation of Umklapp processes in noncrystalline materials

Tullio Scopigno,[1] Matteo D'astuto,[2] Michael Krisch,[2] Giancarlo Ruocco,[3] and Francesco Sette[2]
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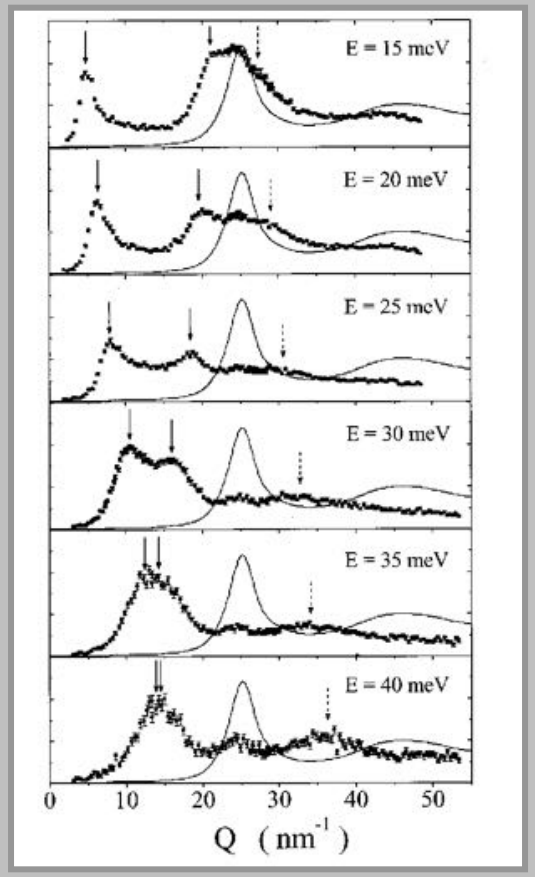
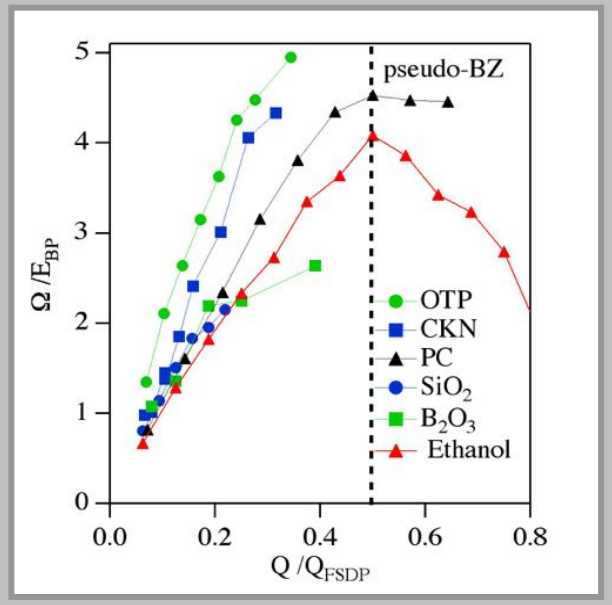
(Received 2 January 2001; published 5 June 2001)





VOLUME 85, NUMBER 6 PHYSICAL REVIEW LETTERS 7 AUGUST 2000

Experimental Evidence of the Acousticlike Character of the High Frequency Excitations in Glasses

C. Masciovecchio,[1] A. Mermet,[2] G. Ruocco,[3] and F. Sette[4]
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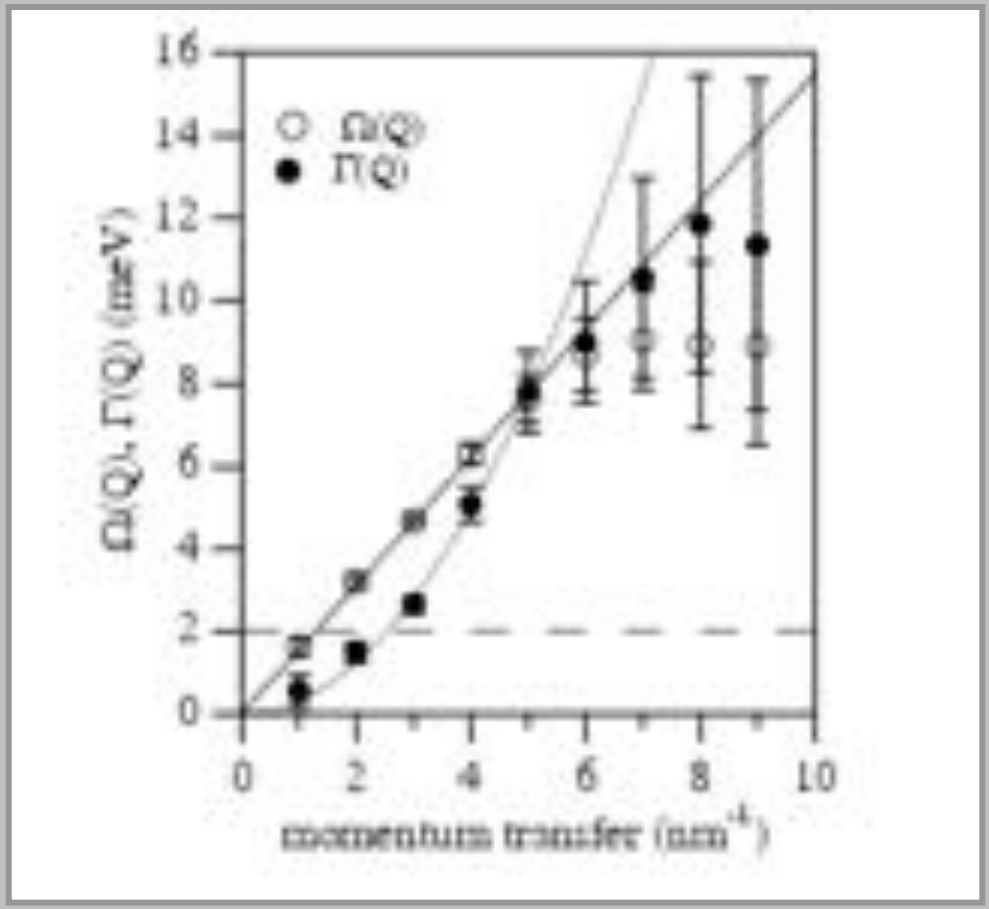
[4]*European Synchrotron Radiation Facility, B.P. 220, F-38043 Grenoble Cedex, France*
(Received 22 February 2000)

4 – Broadening at small Q : Γ(Q) < Ω(Q)



INSTITUTE OF PHYSICS PUBLISHING — JOURNAL OF PHYSICS: CONDENSED MATTER

J. Phys.: Condens. Matter 15 (2003) S1259–S1267 — PII: S0953-8984(03)58099-7

High-frequency collective excitations in a molecular glass-former

J Mattsson[1], A Matic[2], G Monaco[3], D Engberg[4] and L Börjesson[2]

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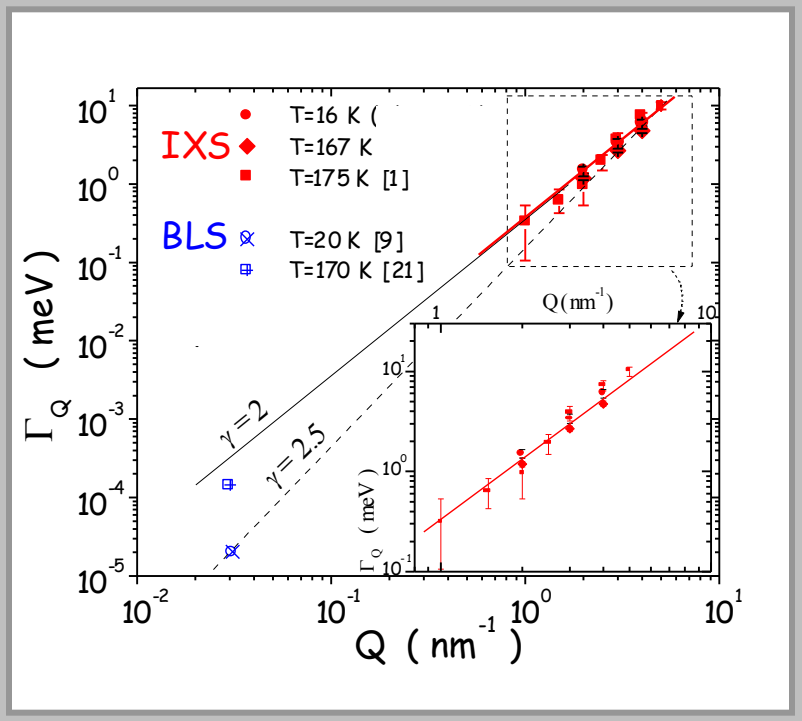
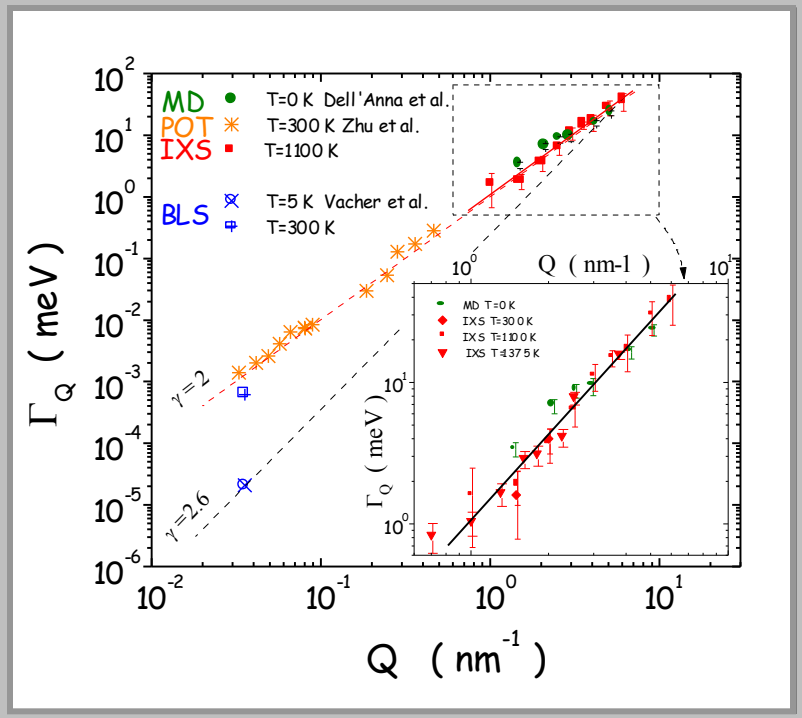
[3] European Synchrotron Radiation Facility, BP 220, F-38043, Grenoble Cedex, France
[4] The Studsvik Neutron Research Laboratory, SE-611 82 Nyköping, Sweden

Propylene Carbonate

5 – Broadening at small Q : $\Gamma(Q) \propto Q^2$



Glycerol



v-silica

6 – Broadening T-independent

VOLUME 83, NUMBER 26 PHYSICAL REVIEW LETTERS 27 DECEMBER 1999

Nondynamic Origin of the High-Frequency Acoustic Attenuation in Glasses

G. Ruocco,[1] F. Sette,[2] R. Di Leonardo,[1] D. Fioretto,[3] M. Krisch,[2] M. Lorenzen,[2] C. Masciovecchio,[2]
G. Monaco,[1] F. Pignon,[2] and T. Scopigno[4]
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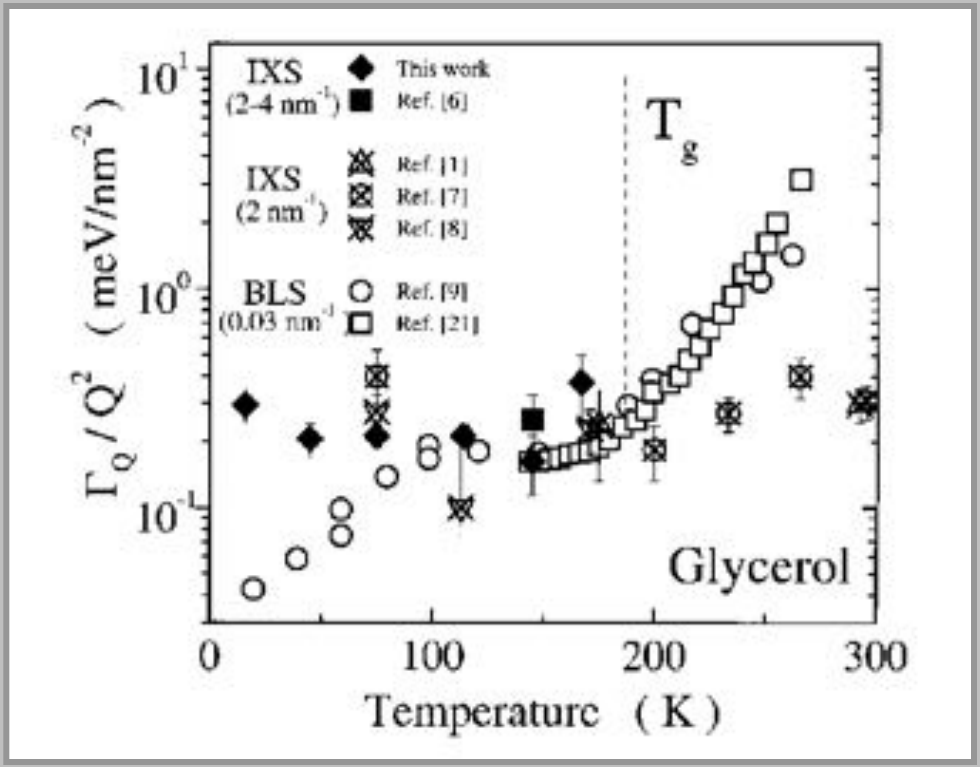
(Received 14 June 1999)

Glycerol



7 – "Transverse" excitations

PHYSICAL REVIEW B 69, 100201(R) (2004)

Evidence of anomalous dispersion of the generalized sound velocity in glasses

B. Ruzicka,[1] T. Scopigno,[1] S. Caponi,[2] A. Fontana,[3] O. Pilla,[3] P. Giura,[4] G. Monaco,[4] E. Pontecorvo,[1] G. Ruocco,[1] and F. Sette[4]
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(Received 8 January 2004; published 12 March 2004)

INSTITUTE OF PHYSICS PUBLISHING — JOURNAL OF PHYSICS: CONDENSED MATTER
J. Phys.: Condens. Matter **15** (2003) S1269–S1278 — PII: S0953-8984(03)58352-7

High-frequency transverse dynamics in glasses

T Scopigno[1], E Pontecorvo[1], R Di Leonardo[1], M Krisch[2], G Monaco[2], G Ruocco[1], B Ruzicka[1] and F Sette[2]

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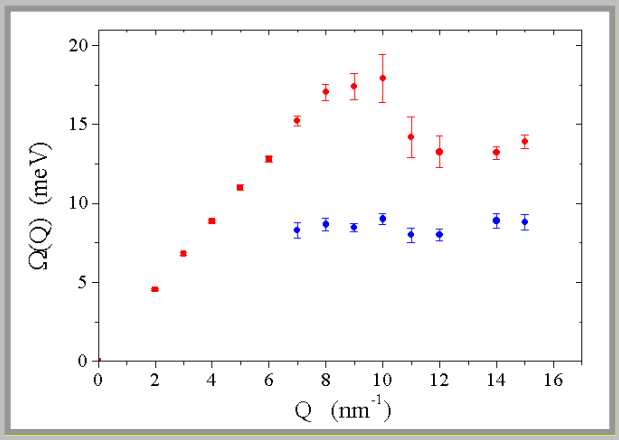

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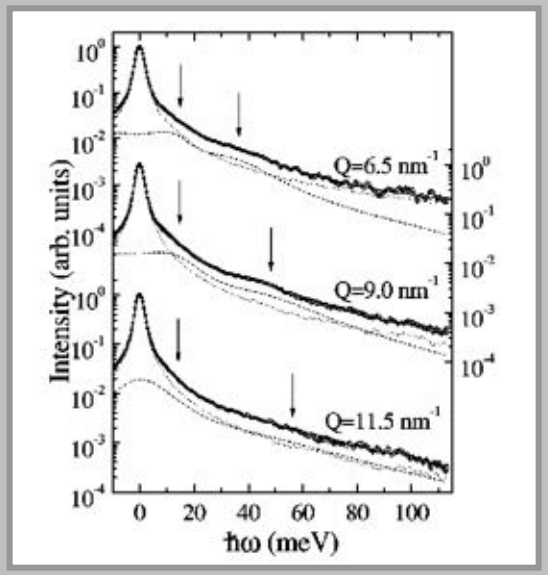
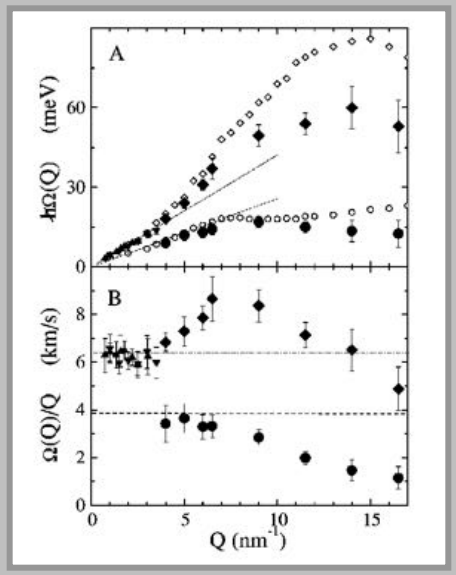
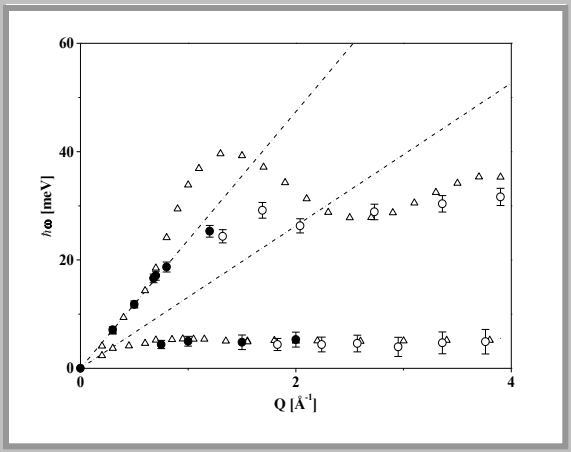




SiO_2



GeO_2

8 – Positive Dispersion of the sound velocity

PHYSICAL REVIEW B 69, 100201(R) (2004)

Evidence of anomalous dispersion of the generalized sound velocity in glasses

B. Ruzicka,[1] T. Scopigno,[1] S. Caponi,[2] A. Fontana,[3] O. Pilla,[3] P. Giura,[4] G. Monaco,[4] E. Pontecorvo,[1] G. Ruocco,[1] and F. Sette[4]
[1]*INFM and Dipartimento di Fisica, Universitá di Roma "La Sapienza," 00185 Roma, Italy*
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VOLUME 84, NUMBER 25 PHYSICAL REVIEW LETTERS 19 JUNE 2000

Relaxation Processes in Harmonic Glasses?

G. Ruocco,[1] F. Sette,[2] R. Di Leonardo,[1] G. Monaco,[2] M. Sampoli,[3] T. Scopigno,[4] and G. Viliani[4]
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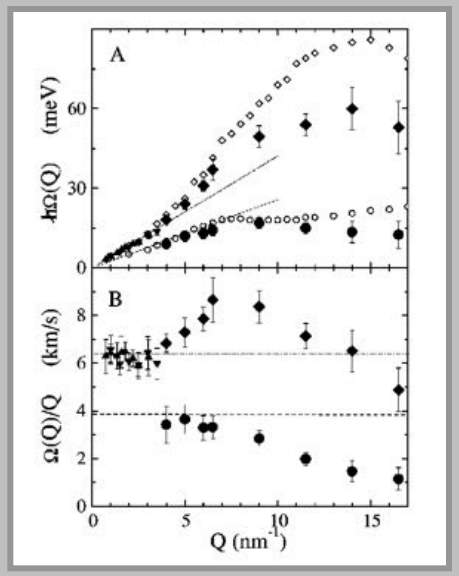
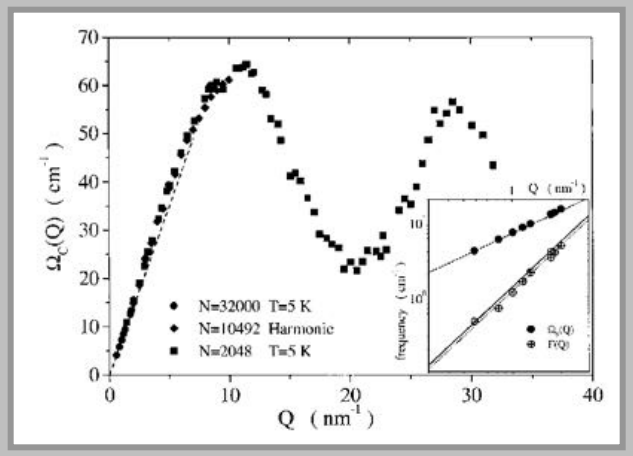
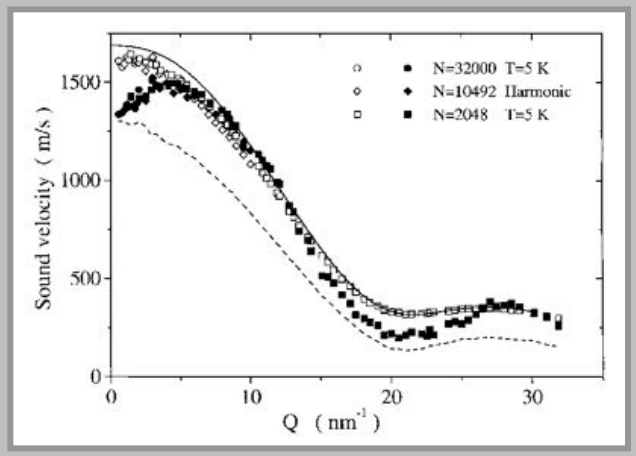
(Received 6 December 1999)





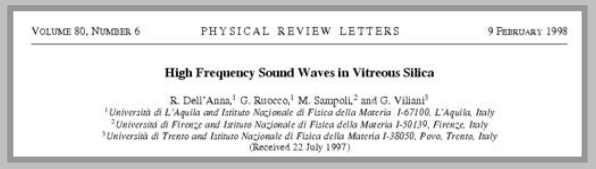


SiO_2

Summary

1 – There exist propagating acoustic-like excitations in glasses $\Omega(Q) = c\,Q$
2 – These excitations exist at energy well above the Boson Peak Energy
3 - The similarity with "phonons" goes beyond the first BZ: Umklap processes
4 – These excitations are well defined at small Q : $\Gamma(Q) < \Omega(Q)$
5 – The excitations' broadening, $\Gamma(Q)$, increase as Q^2: $\Gamma(Q) = d\,Q^2$
6 – The excitations' broadening is T-independent
7 – There exist also "Transverse" excitations
8 – It exists a positive dispersion of the sound velocity

A still open problem



VOLUME 80, NUMBER 6 PHYSICAL REVIEW LETTERS 9 FEBRUARY 1998

High Frequency Sound Waves in Vitreous Silica

R. Dell'Anna,[1] G. Ruocco,[1] M. Sampoli,[2] and G. Viliani[3]

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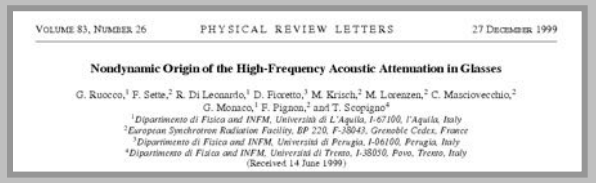
[3]*Università di Trento and Istituto Nazionale di Fisica della Materia I-38050, Povo, Trento, Italy*

(Received 22 July 1997)



VOLUME 83, NUMBER 26 PHYSICAL REVIEW LETTERS 27 DECEMBER 1999

Nondynamic Origin of the High-Frequency Acoustic Attenuation in Glasses

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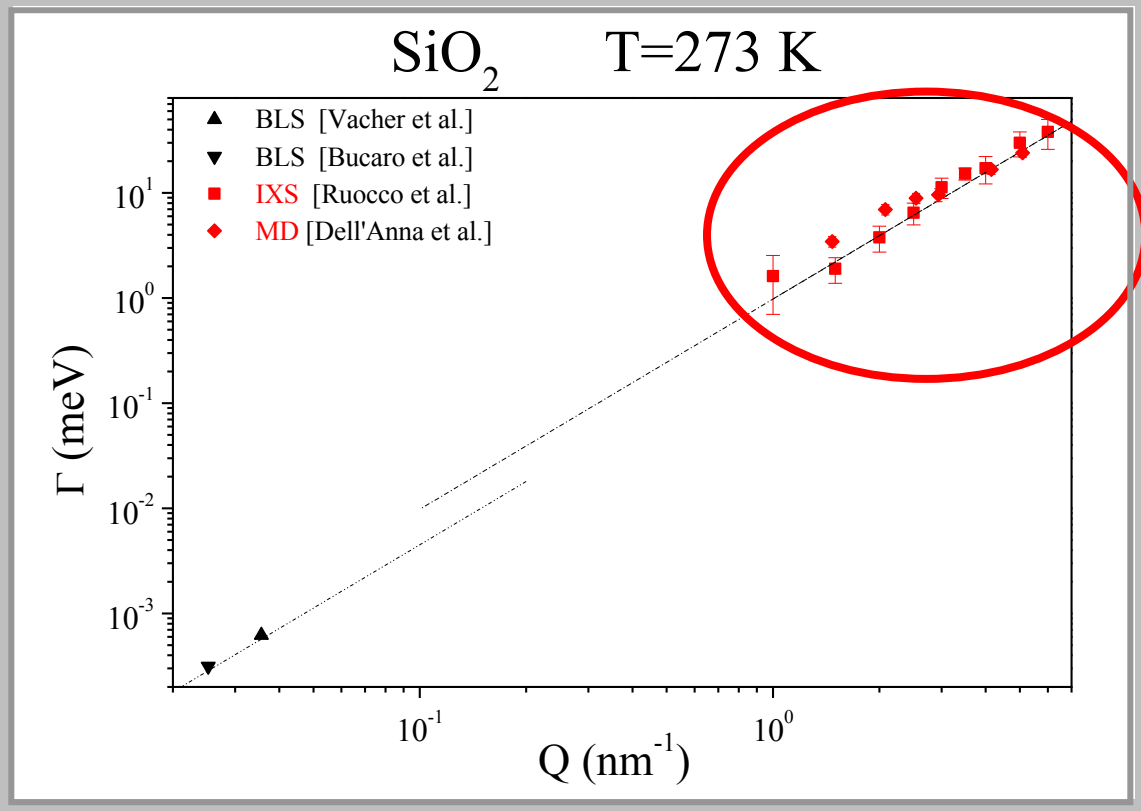
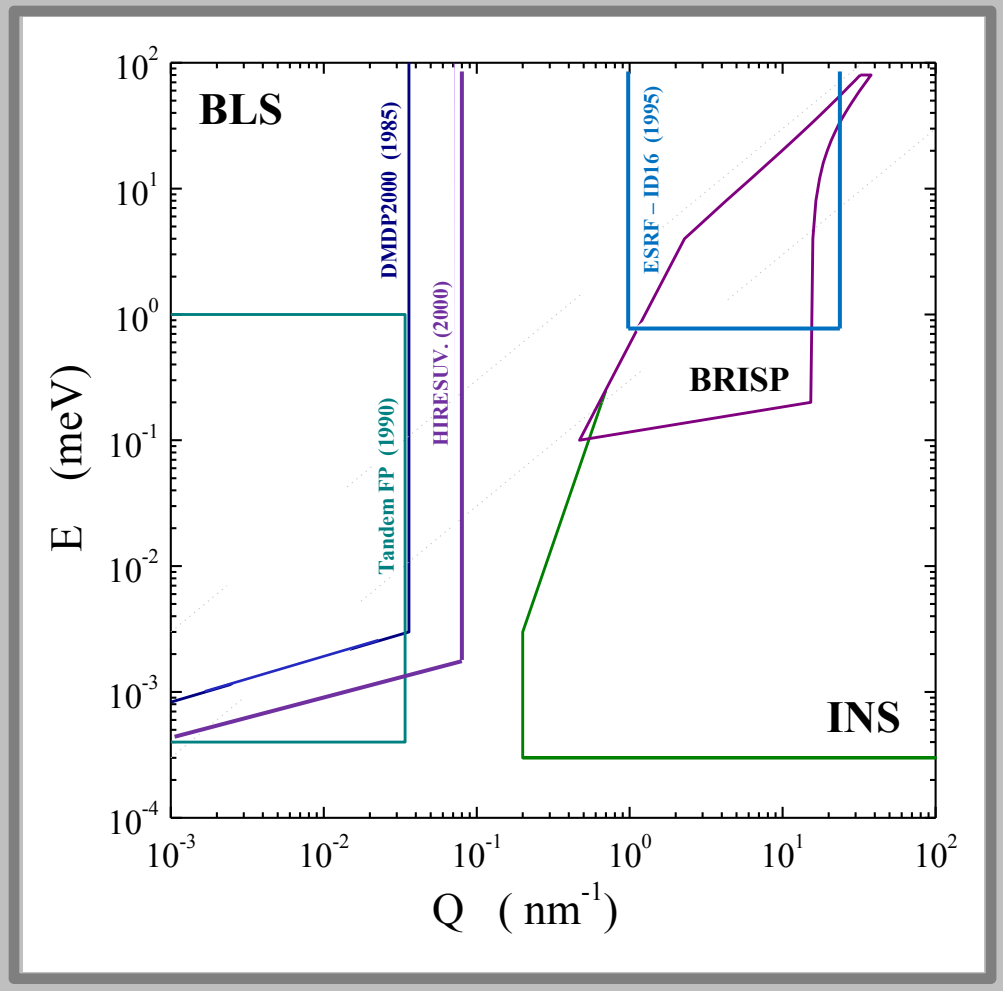
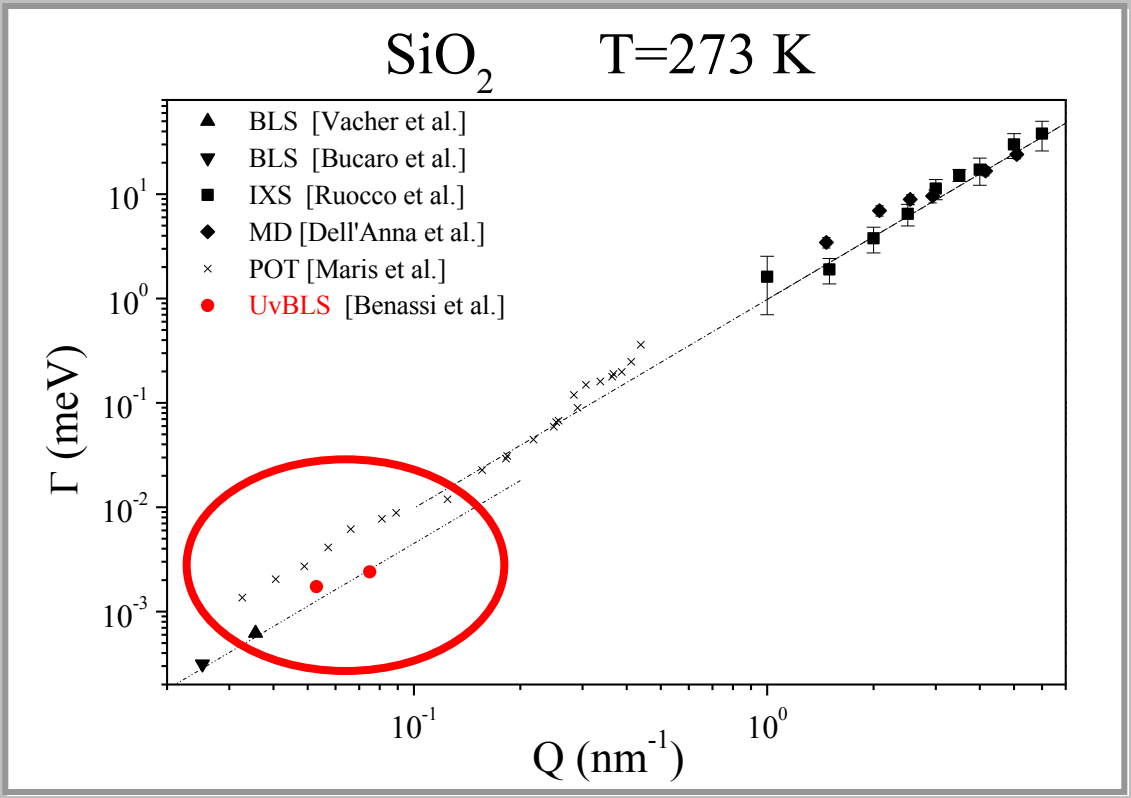
[4]*Dipartimento di Fisica and INFM, Università di Trento, I-38050, Povo, Trento, Italy*

(Received 14 June 1999)



High frequency dynamics in disordered systems





PHYSICAL REVIEW B 71, 172201 (2005)

Sound attenuation in a unexplored frequency region: Brillouin ultraviolet light scattering measurements in *v*-SiO_2

P. Benassi,[1,5] S. Caponi,[2,5] R. Eramo,[3,5] A. Fontana,[2,5] A. Giugni,[1,5] M. Nardone,[1,5] M. Sampoli,[4,5] and G. Viliani[2,5]
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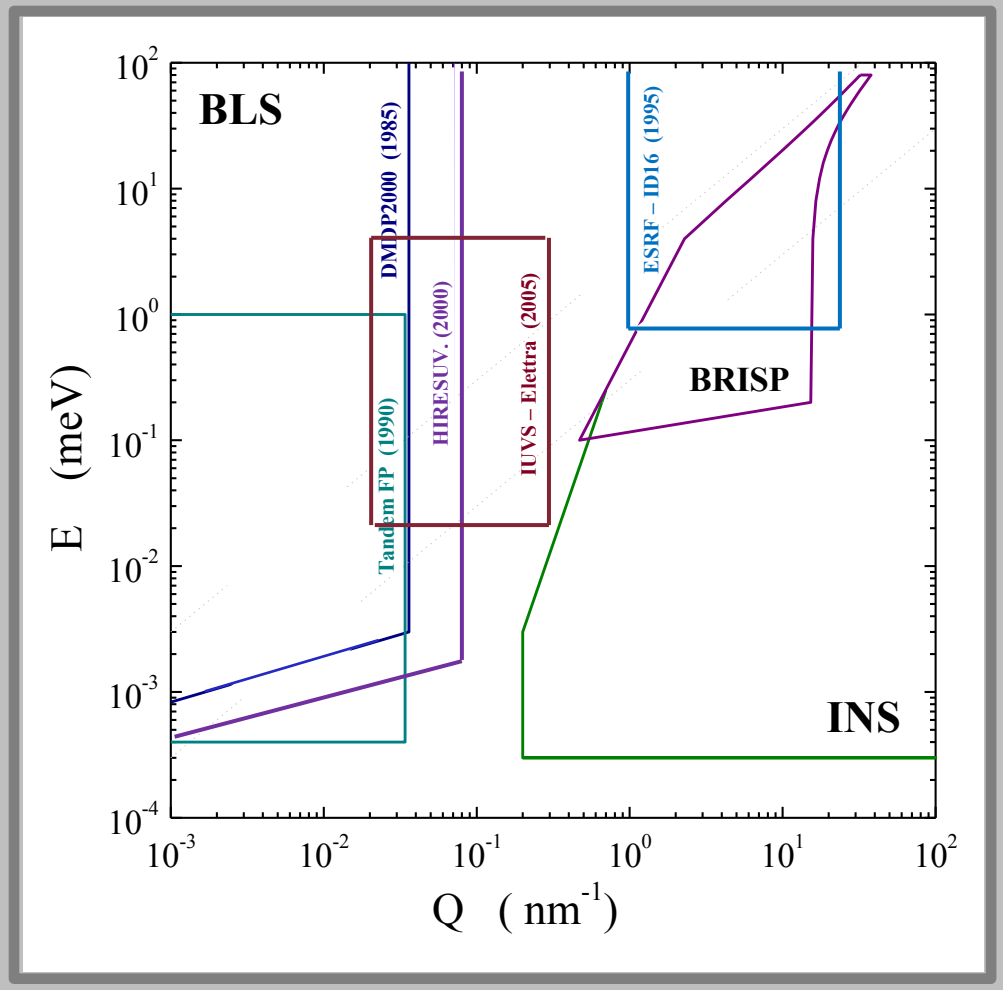
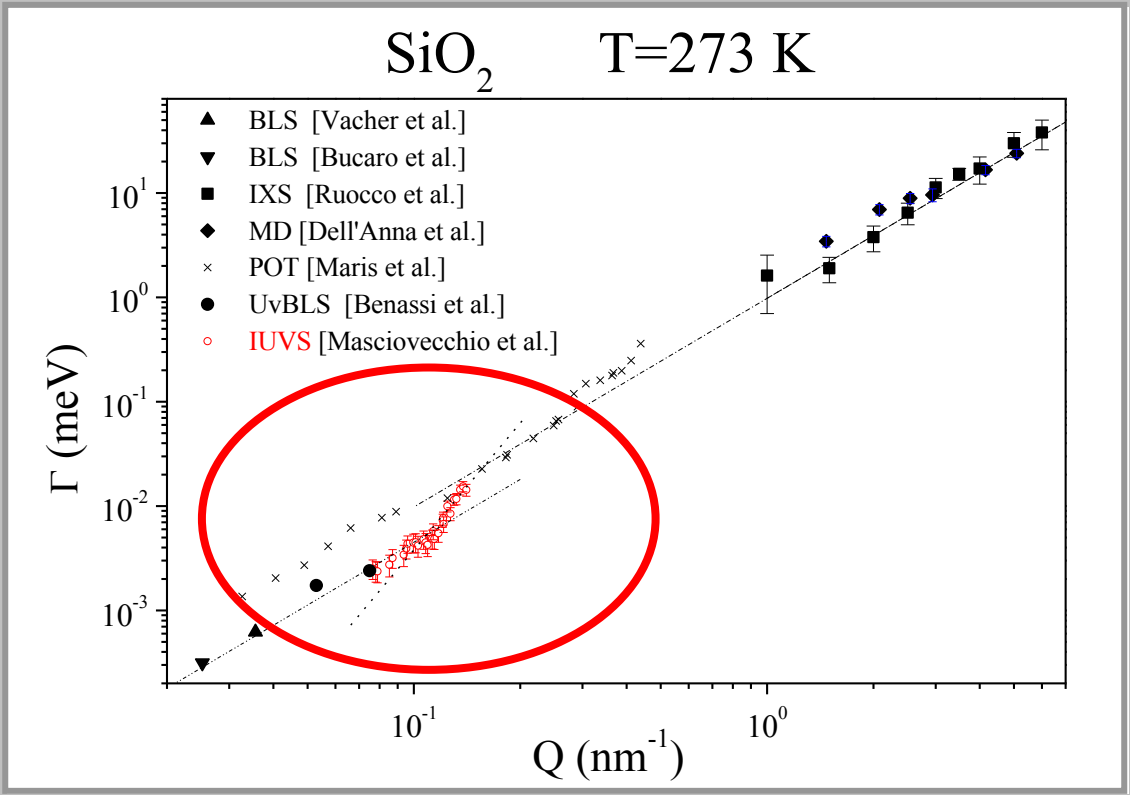
(Received 3 February 2005; published 6 May 2005)

High frequency dynamics in disordered systems



High frequency dynamics in disordered systems



PRL 97, 035501 (2006) PHYSICAL REVIEW LETTERS week ending 21 JULY 2006

Evidence for a Crossover in the Frequency Dependence of the Acoustic Attenuation in Vitreous Silica

C. Masciovecchio,[1] G. Baldi,[2] S. Caponi,[4] L. Comez,[3,4] S. Di Fonzo,[1] D. Fioretto,[3,4] A. Fontana,[2,4] A. Gessini,[1] S. C. Santucci,[1,3] F. Sette,[5] G. Viliani,[2,4] P. Vilmercati,[1] and G. Ruocco[6,4]
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[5]*European Synchrotron Radiation Facility, BP 220, 38043 Grenoble, France*
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(Received 30 August 2005; published 18 July 2006)

Theory

VOLUME 84, NUMBER 25 PHYSICAL REVIEW LETTERS 19 JUNE 2000

Relaxation Processes in Harmonic Glasses?

G. Ruocco,[1] F. Sette,[2] R. Di Leonardo,[1] G. Monaco,[2] M. Sampoli,[3] T. Scopigno,[4] and G. Viliani[4]
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(Received 6 December 1999)

T-independent process(es)

"Disorder induced"
Relaxation Process

$\Gamma(Q) \propto Q^2$ high Q

Rayleigh scattering

$\Gamma(Q) \propto Q^4$ low Q

a *harmonic system* suggests the use of formalism that describes the density correlators $\phi(Q,t) = F(Q,t)/S(Q)$ through its generalized Langevin equation [16]:

$$\ddot{\phi}(Q,t) + \omega_o^2 \phi(Q,t) + \int_o^t m(Q,t-t') \times \dot{\phi}(Q,t')\, dt = 0, \quad (5)$$

where $\omega_o^2 = K_B T Q^2 / M S(Q)$ and $m(Q,t)$ is the "memory function." This equation has been rigorously derived for ergodic systems but, as recently shown in the framework of

$$S^{(1)}(Q,\omega) = \frac{K_B T Q^2}{\pi M} \lim_{s\to 0} \Sigma_p \frac{E_p(Q)}{\omega_p^2} \frac{s}{s^2 + (\omega - \omega_p)^2}, \quad (10)$$

and comparing Eqs. (10) and (9) one gets [18]

$$\Gamma_Q = v_o^4 Q^2 \frac{\pi M}{K_B T} \lim_{\omega\to 0} S(Q,\omega). \quad (11)$$

Similarly,

$$\tau_\alpha \approx \frac{v_o^4}{(\ldots)} \frac{\pi M}{K_B T} \lim_{\omega\to 0} S(Q,\omega). \quad (10)$$

Theory

PRL 98, 025501 (2007) PHYSICAL REVIEW LETTERS week ending 12 JANUARY 2007

Acoustic Attenuation in Glasses and its Relation with the Boson Peak

W. Schirmacher,[1] G. Ruocco,[2,3] and T. Scopigno[3]
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[2]Dipartimento di Fisica, Università di Roma "La Sapienza", I-00185, Roma, Italy
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(Received 24 August 2006; published 9 January 2007)

$$\omega_D \Delta g(\omega) \doteq \omega_D [g(\omega) - g_D(\omega)] = f(c_L, c_T) \frac{\Gamma(\omega)}{\omega_D} \quad (5)$$

with

$$f(c_L, c_T) = \frac{2}{\pi} \left(\frac{c_D}{c_L}\right)^2 \left[1 + \left(\frac{c_L}{c_T}\right)^4\right] \quad (6)$$

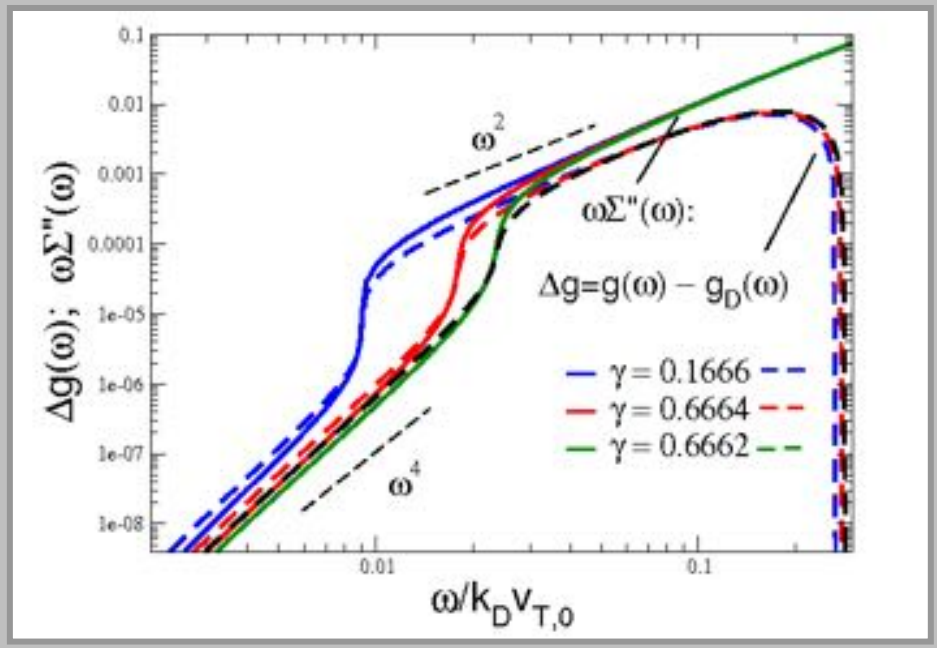


Table I

Material	V/N	c_L	c_T	A	B
	A^{-3}	m/s	m/s	ps^3	ps
MD-LJ	39.5	1320 [16]	540 [34]	2.1 10^{-2} [34]	0.120 [16]
MD-SiO_2	14.1	5940 [17]	3570 [17]	3.7 10^{-5} [17]	0.045 [17]
SiO_2	15.1	5960 [9]	3750 [9]	5.3 10^{-5} [35]	0.042 [4]
GeO_2	16.1	3650 [36]	2150 [36]	1.4 10^{-4} [37]	0.034 [37]
Glycerol	8.2	3600 [38]	1870 [38]	9.9 10^{-5} [39]	0.031 [40]
oTP	10.7	2940 [41]	1370 [41]	3.5 10^{-4} [41]	0.036 [40]
Selenium	30.0	1800 [42]	895 [42]	2.2 10^{-3} [43]	0.070 [44]

Table II

Material	k_D	c_D	ω_D	A_D
	A^{-1}	m/s	ps	ps^3
MD-LJ	1.14	610	6.99	8.8 10^{-3}
MD-SiO_2	1.61	3950	63.7	1.2 10^{-5}
SiO_2	1.58	4130	65.1	1.1 10^{-5}
GeO_2	1.54	2380	36.8	6.0 10^{-5}
Glycerol	1.93	2090	40.4	4.5 10^{-5}
oTP	1.77	1540	27.3	1.5 10^{-4}
Selenium	1.25	1000	12.6	1.5 10^{-3}

Table III

Material	ρ	R_{Exp}	R_{Th}	Err
		ps^2	ps^2	%
MD-LJ	2.4	0.099	0.103	2
MD-SiO_2	3.1	0.00055	0.00060	4
SiO_2	4.9	0.00101	0.00053	32
GeO_2	2.3	0.00237	0.00187	12
Glycerol	2.2	0.00177	0.00194	5
oTP	2.4	0.00445	0.00523	8
Selenium	1.4	0.00935	0.02170	40

Disordered systems - Thanks

1. High frequency excitation in glasses: Expanding in the Q-omega region

Francesco Sette (ESRF)
Walter Schirmacher (UniMainz)
Giulio Monaco (UniTN)
Tullio Scopigno (Sapienza)
Claudio Masciovecchio (Elettra)
…
Too many others….

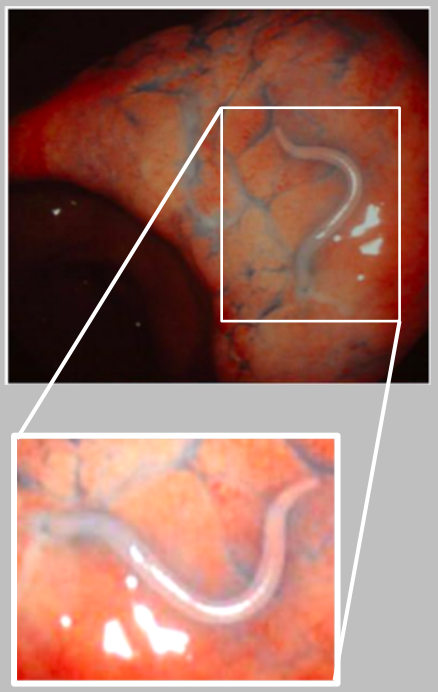
2. Diagnosis of tumors via animal based biosensors

Surg Today (2015) 45:1321–1325
DOI 10.1007/s00595-014-1012-3

CASE REPORT

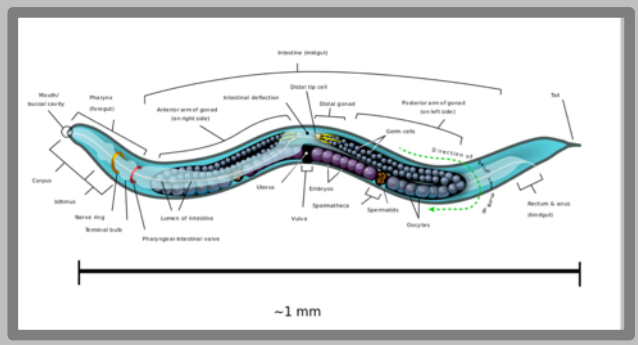
An anisakis larva attached to early gastric cancer: report of a case

Hideto Sonoda · Kazuharu Yamamoto · Kazuyuki Ozeki · Humio Inoye · Shuji Toda · Yoshihiko Maehara



Caenorhabditis elegans

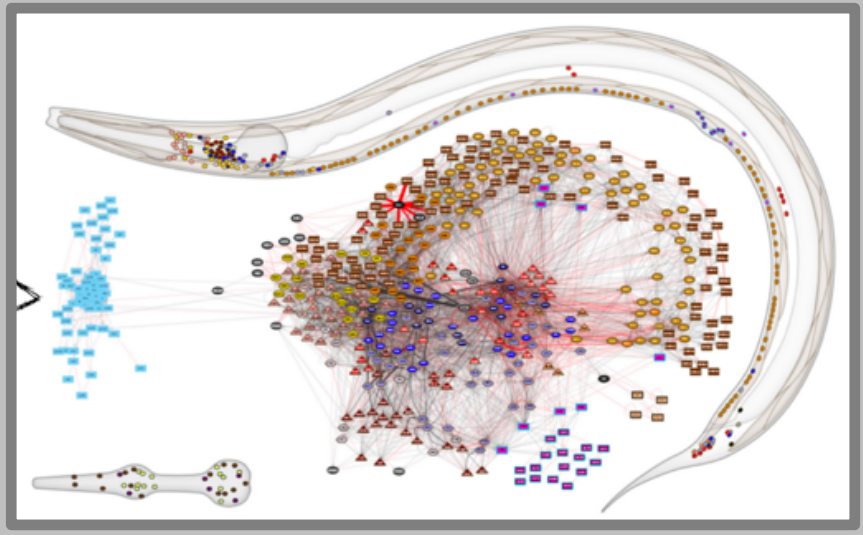
1. Model in biology: the simplest pluricellular organism
2. 1 mm length, 0.05 mm diameter
3. Transparent body
4. feed: Escherichia coli
5. hermaphrodite (genetic stability)
6. 20.000 genes (humans: 30.000/40.000 genes)

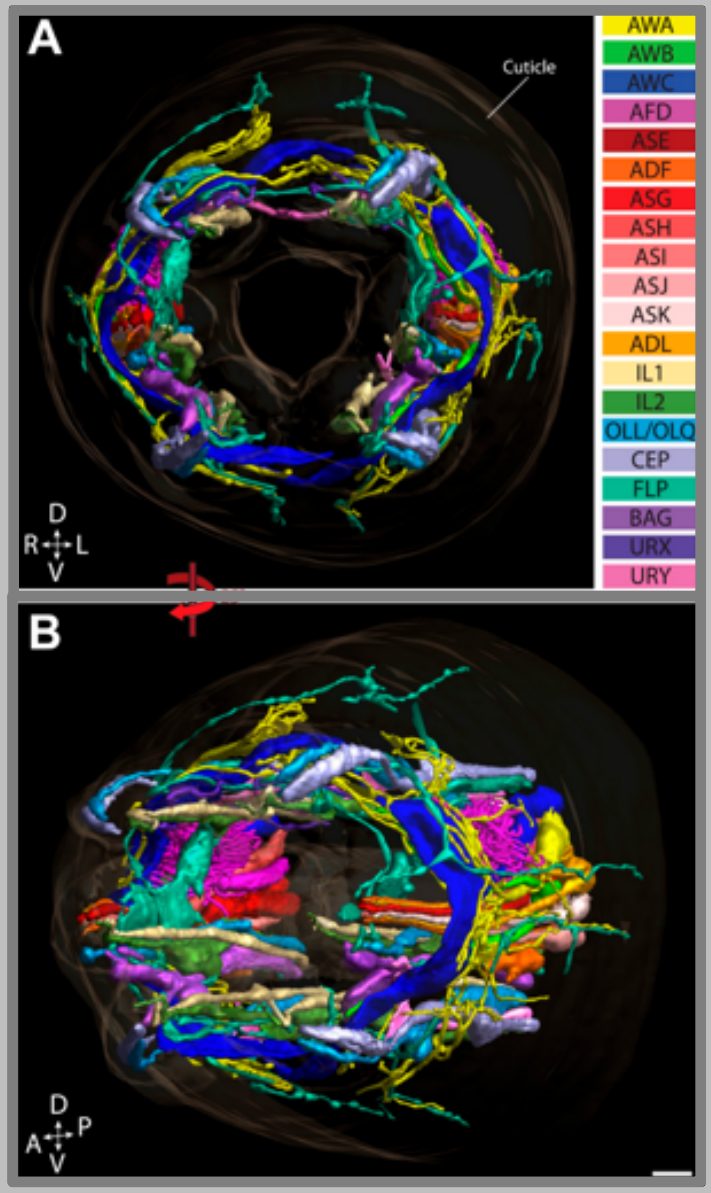


Diagnosis of Tumors via animal based biosensors

Caenorhabditis elegans

1. Model in biology
2. 1 mm length, 0.05 mm diameter
3. Transparent body
4. feed: Escherichia coli
5. hermaphrodite (genetic stability)
6. 20.000 genes
7. Fixed cells number: 959
8. Fixed neurons number: 302
9. Well known connectome: 7000 synapses





Diagnosis of Tumors via animal based biosensors

RESEARCH ARTICLE

A Highly Accurate Inclusive Cancer Screening Test Using *Caenorhabditis elegans* Scent Detection

Takaaki Hirotsu[1,2,3,4¤a]*, Hideto Sonoda[3,5,7¤a]*, Takayuki Uozumi[1], Yoshiaki Shinden[5], Koshi Mimori[6], Yoshihiko Maehara[7], Naoko Ueda[4], Masayuki Hamakawa[1]

1 Graduate School of Systems Life Sciences, Kyushu University, Fukuoka, Japan, **2** Department of Biology, Graduate School of Sciences, Kyushu University, Fukuoka, Japan, **3** Division of Applied Medical Sensing, Research and Development Center for Taste and Odor Sensing, Kyushu University, Fukuoka, Japan, **4** Department of Biology, Faculty of Science, Kyushu University, Fukuoka, Japan, **5** Department of General Surgery, Imari-Arita Kyoritsu Hospital, Saga, Japan, **6** Department of Surgery, Kyushu University Beppu Hospital, Oita, Japan, **7** Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

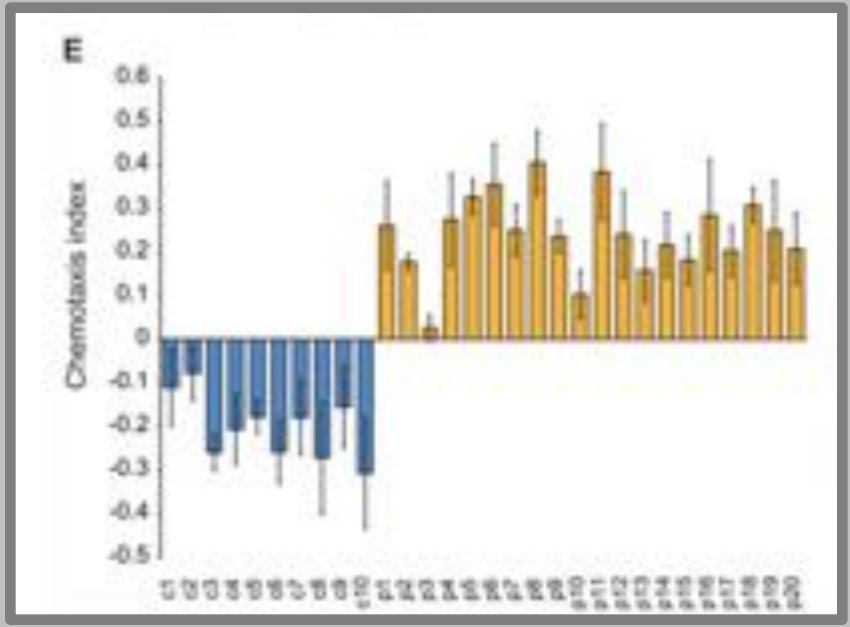
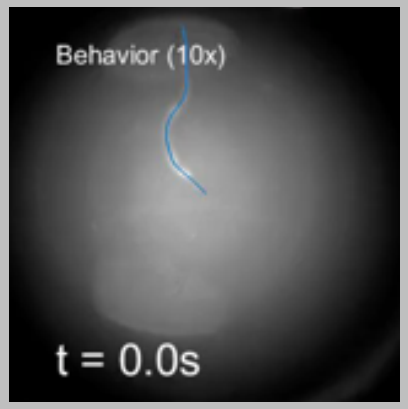


Table 1. Accuracy of tumour markers in extended characteri

	Stage	n	Cl
Oesophageal ca.	0	1	0
	Total	1	0
Gastric ca.	I	4	0
	IV	1	1
	Total	5	1
Colorectal ca.	0	2	1
	I	1	0
	II	2	0
	III	4	1
	IV	1	1
	Total	10	3
Breast ca.	I	2	0
	II	3	1
	Total	5	1
Pancreatic ca.	IV	1	1
	Total	1	1
Bile duct ca.	I	1	0
	Total	1	0
Prostate ca.	I	1	0
	Total	1	0
All cancers	0	3	1
	I	9	0
	II	5	1
	III	4	1
	IV	3	3
	Total	24	6

Diagnosis of Tumors via animal based biosensors

Neurons – In vivo – C.E.



PNAS

Whole-brain calcium imaging with cellular resolution in freely behaving *Caenorhabditis elegans*

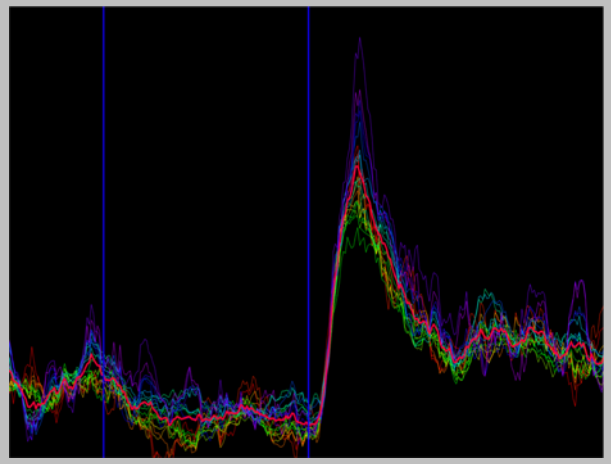
Jeffrey P. Nguyen[a,b,1], Frederick B. Shipley[a,1], Ashley N. Linder[c], George S. Plummer[a], Mochi Liu[a], Sagar U. Setru[a], Joshua W. Shaevitz[a,b], and Andrew M. Leifer[a,2]

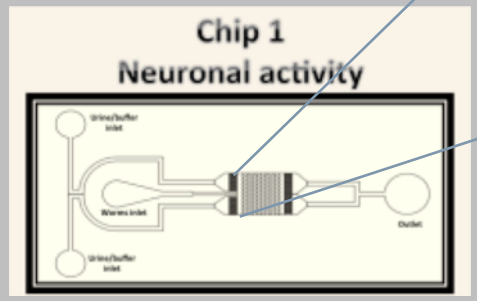
[a]Lewis-Sigler Institute for Integrative Genomics, Princeton University, Princeton, NJ 08544; [b]Department of Physics, Princeton University, Princeton, NJ 08544; and [c]Princeton Neuroscience Institute, Princeton University, Princeton, NJ 08544

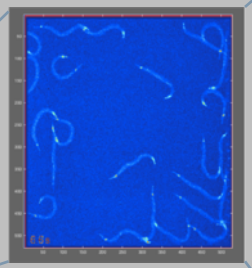
Edited by William Bialek, Princeton University, Princeton, NJ, and approved September 30, 2015 (received for review April 11, 2015)

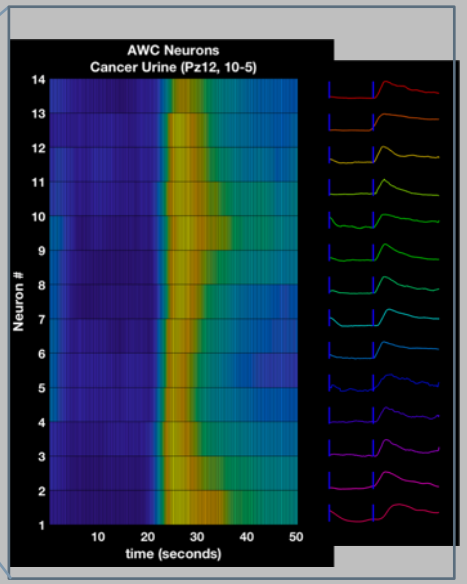
Diagnosis of Tumors via animal based biosensors

Fluorescence signal from AWC neuron

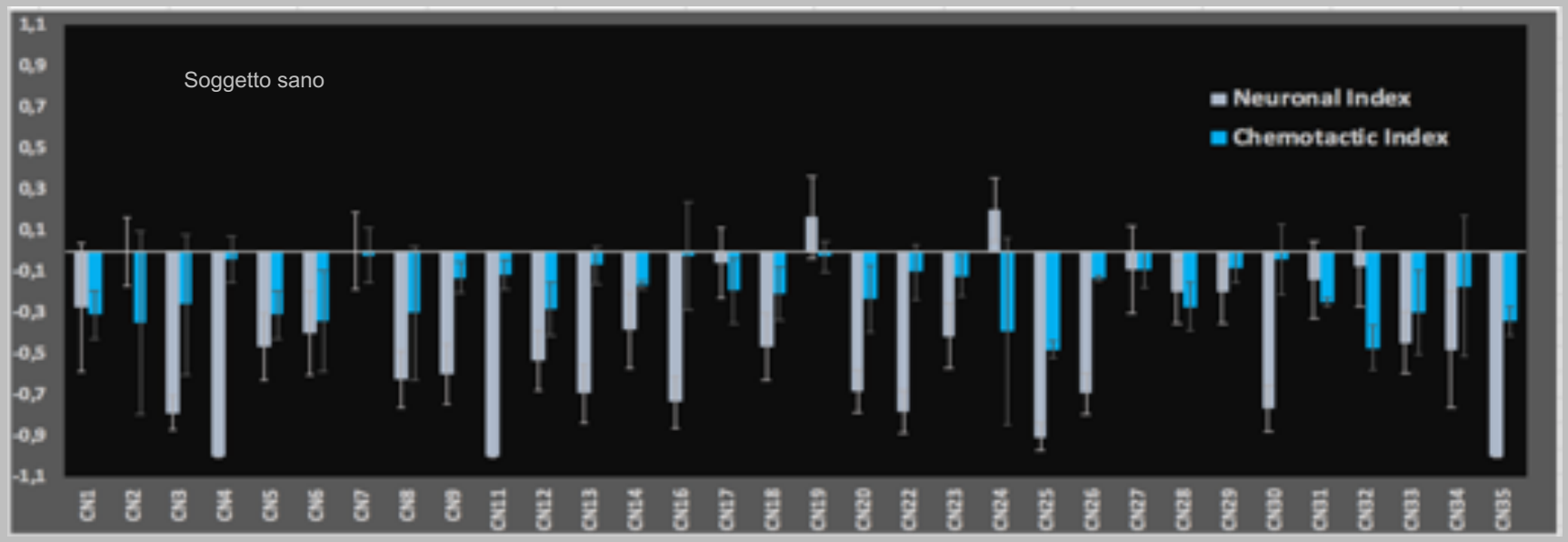


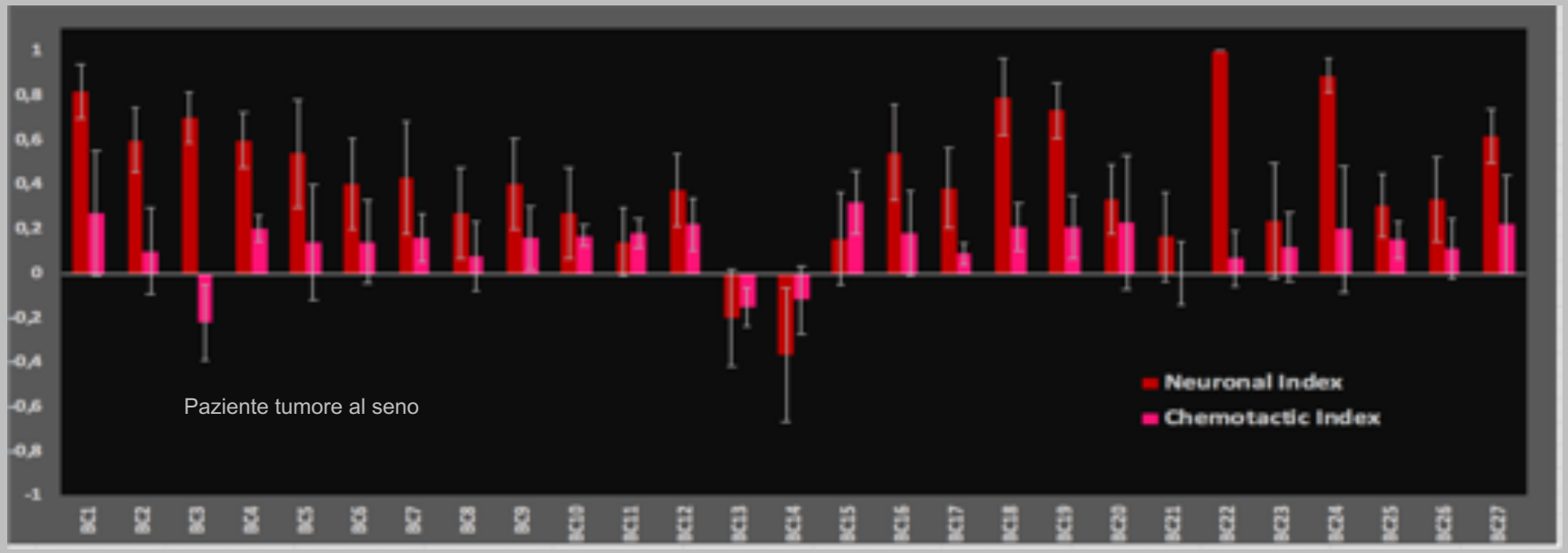




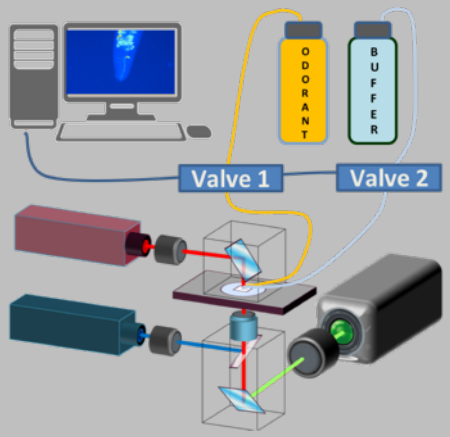


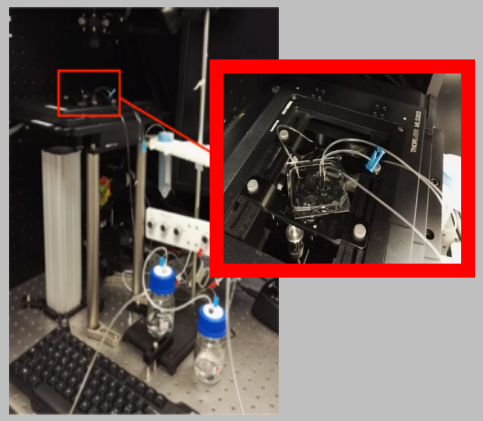
Diagnosis of Tumors via animal based biosensors

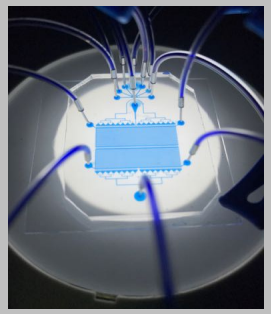


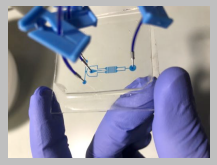


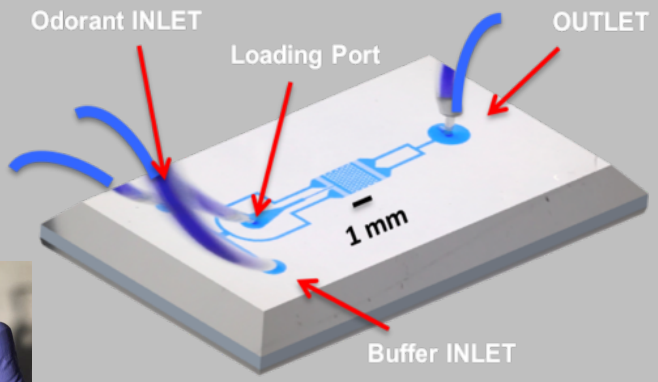
Diagnosis of Tumors via animal based biosensors

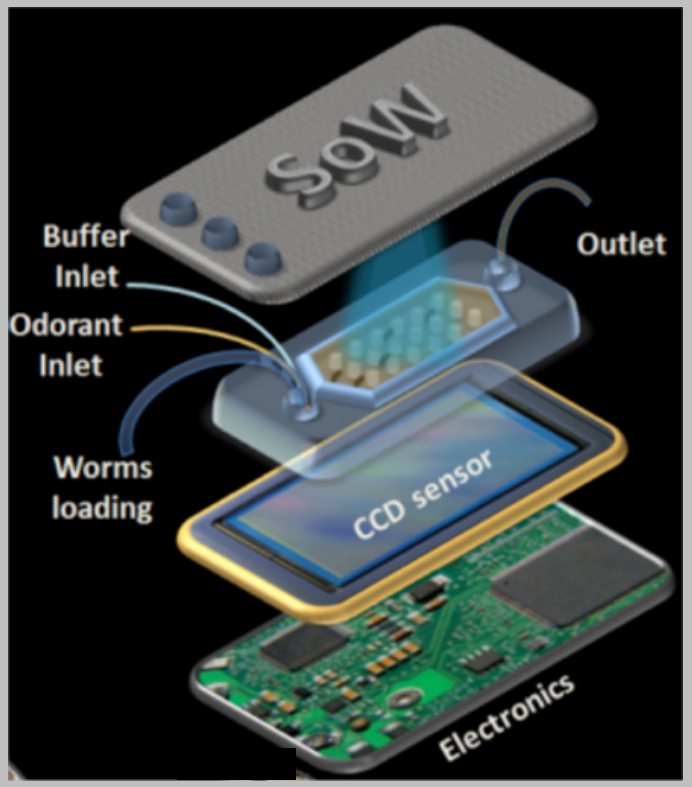








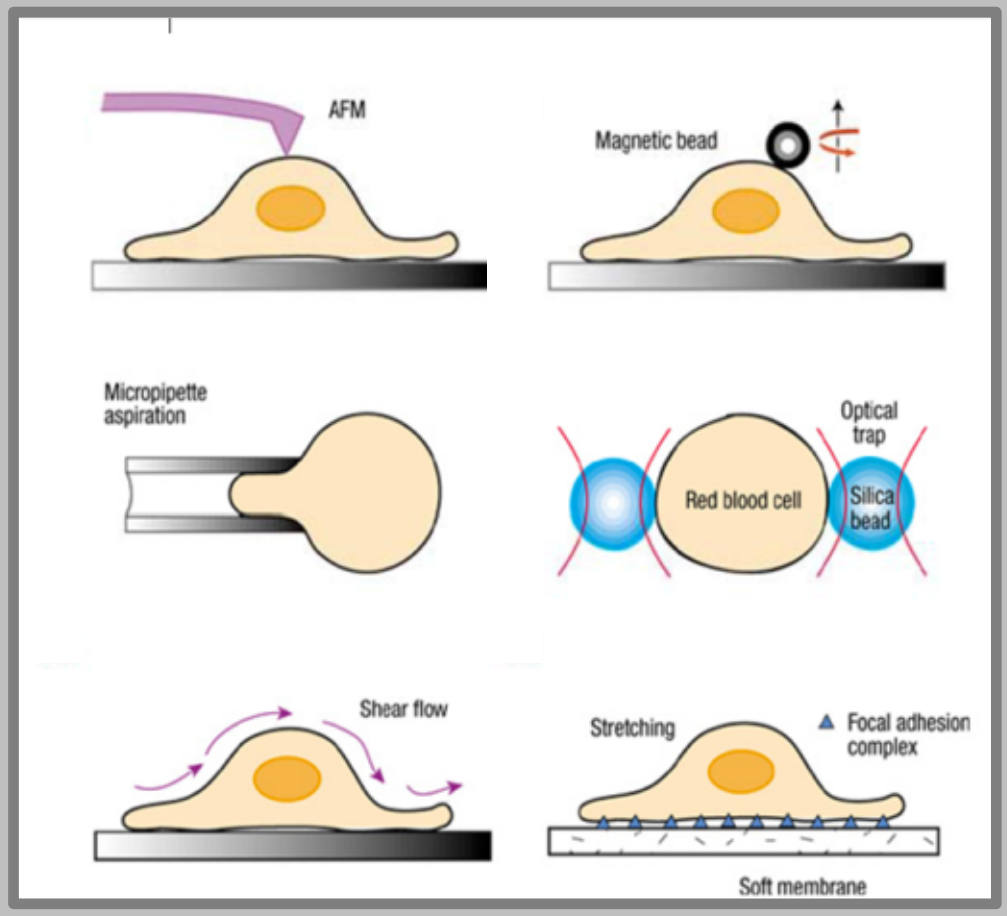




3. New dimension in microscopy: imaging mechanical properties

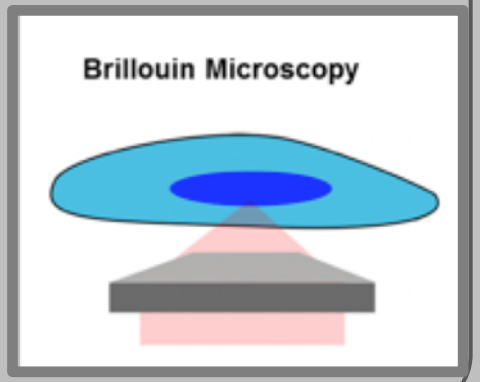
- Biomechanics are crucial in the onset of several diseases (e.g **cancer**, **atherosclerosis**, **glaucoma**, **amyotrophic lateral sclerosis**)

- Existing methods to measure the biomechanics require **contact forces**
  - Invasive
  - Unable to perform 3D imaging
  - cannot provide a subcellular spatial resolution

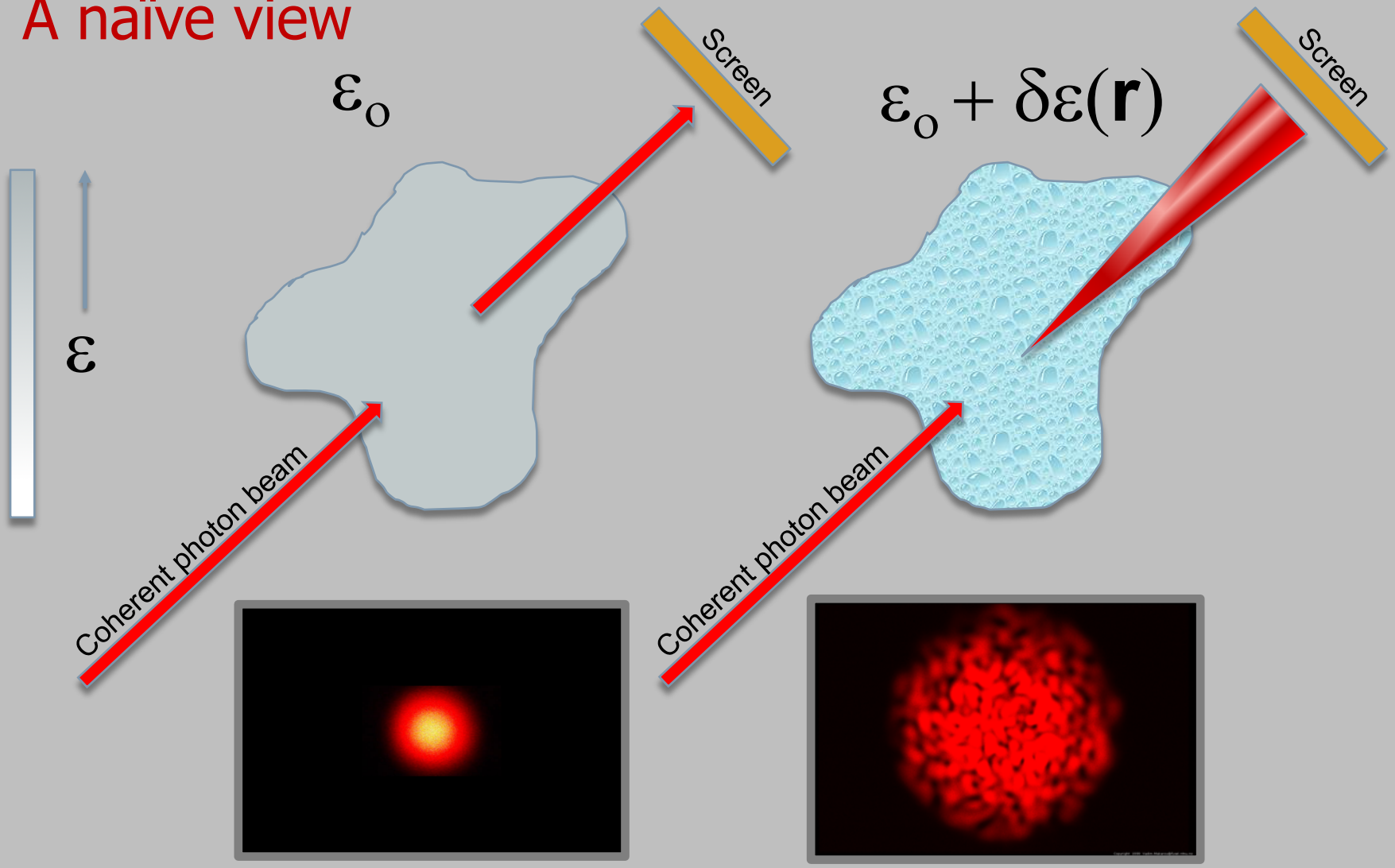


Brillouin Microscopy

- Contactless
- Label Free
- 3D Capability
- New dimension in imaging



A naïve view

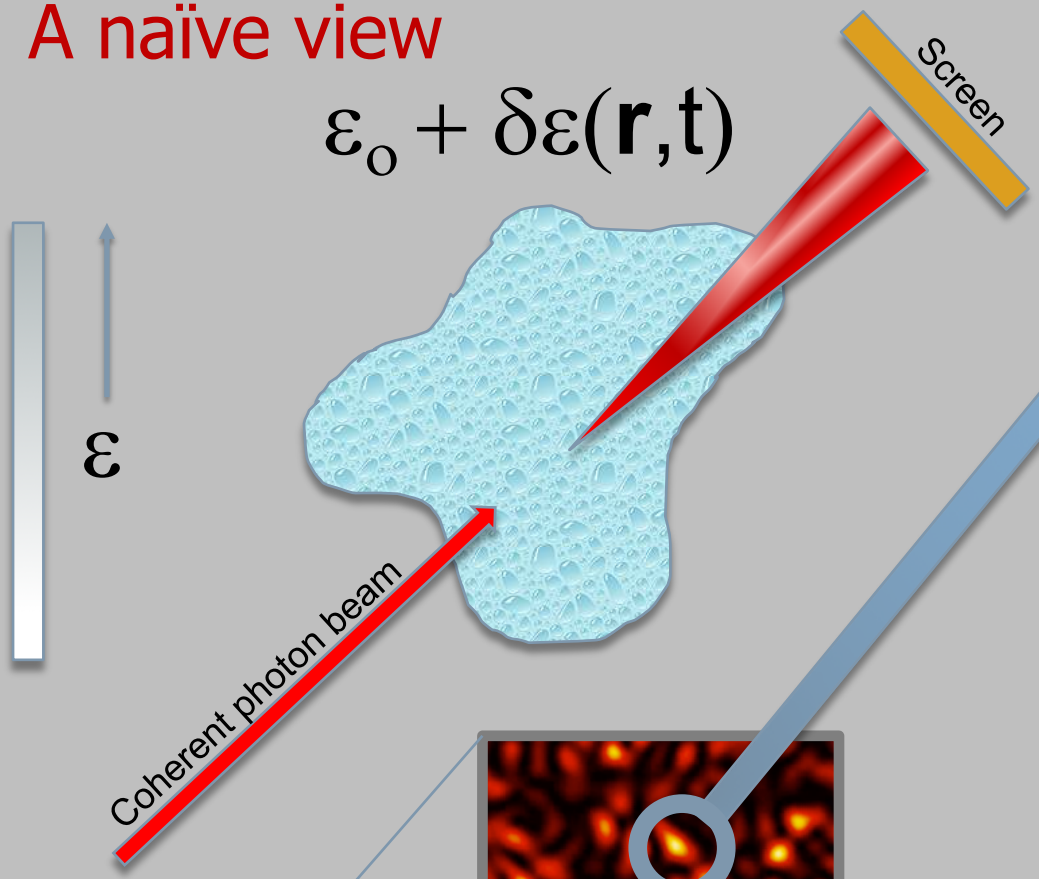


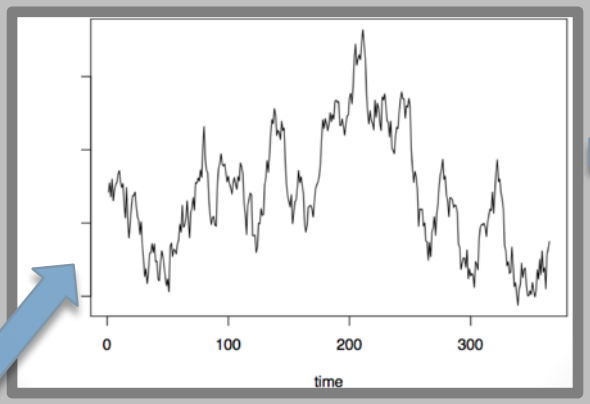
Beam cross section

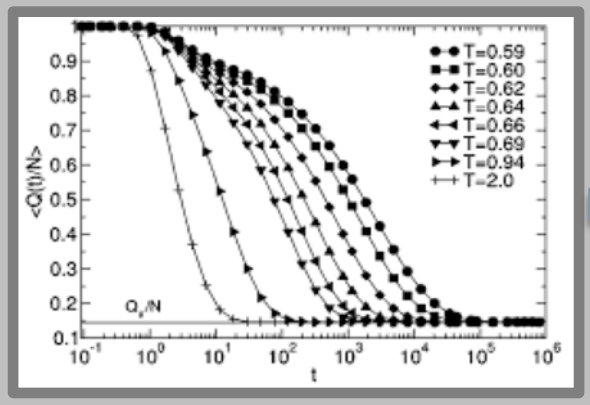
Speckles field

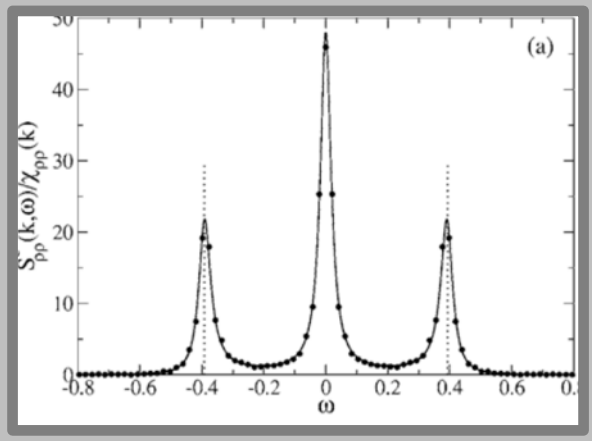
A naïve view

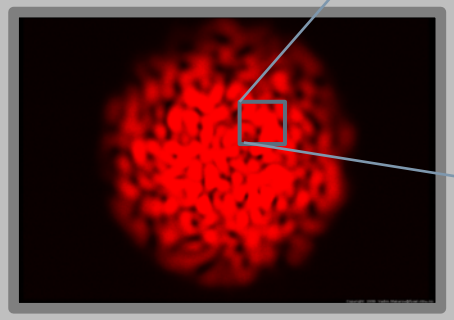
$$\varepsilon_o + \delta\varepsilon(\mathbf{r},t)$$

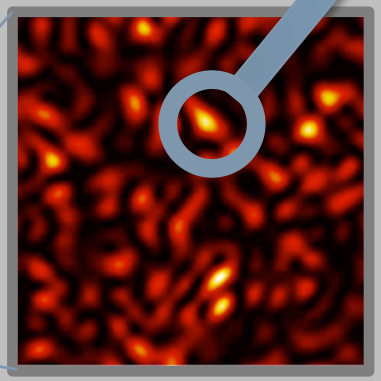


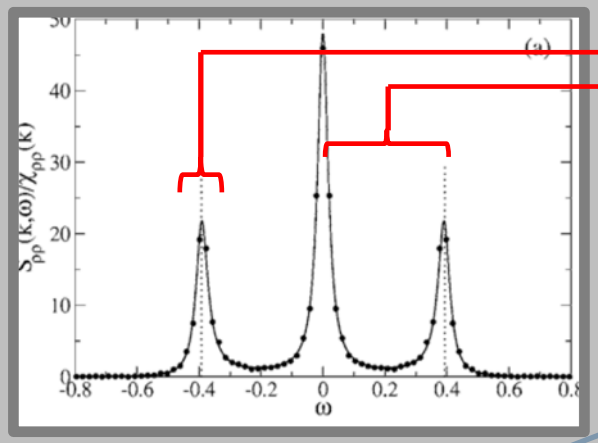












$$S_{\rho\rho}(\mathbf{q},\omega) = \frac{1}{\pi} V\rho^2 k_B T \chi_T \left\{ \left(1 - \frac{1}{\gamma}\right) \left[\frac{D_T q^2}{\omega^2 + [D_T q^2]^2} \right] + \frac{1}{\gamma} \left(\frac{\Gamma q^2}{[\omega - \omega(q)]^2 + [\Gamma q^2]^2} + \frac{\Gamma q^2}{[\omega + \omega(q)]^2 + [\Gamma q^2]^2} \right) + \frac{1}{\gamma} b(q) \left(\frac{[\omega + \omega(q)]}{[\omega + \omega(q)]^2 + [\Gamma q^2]^2} - \frac{[\omega - \omega(q)]}{[\omega - \omega(q)]^2 + [\Gamma q^2]^2} \right) \right\}$$

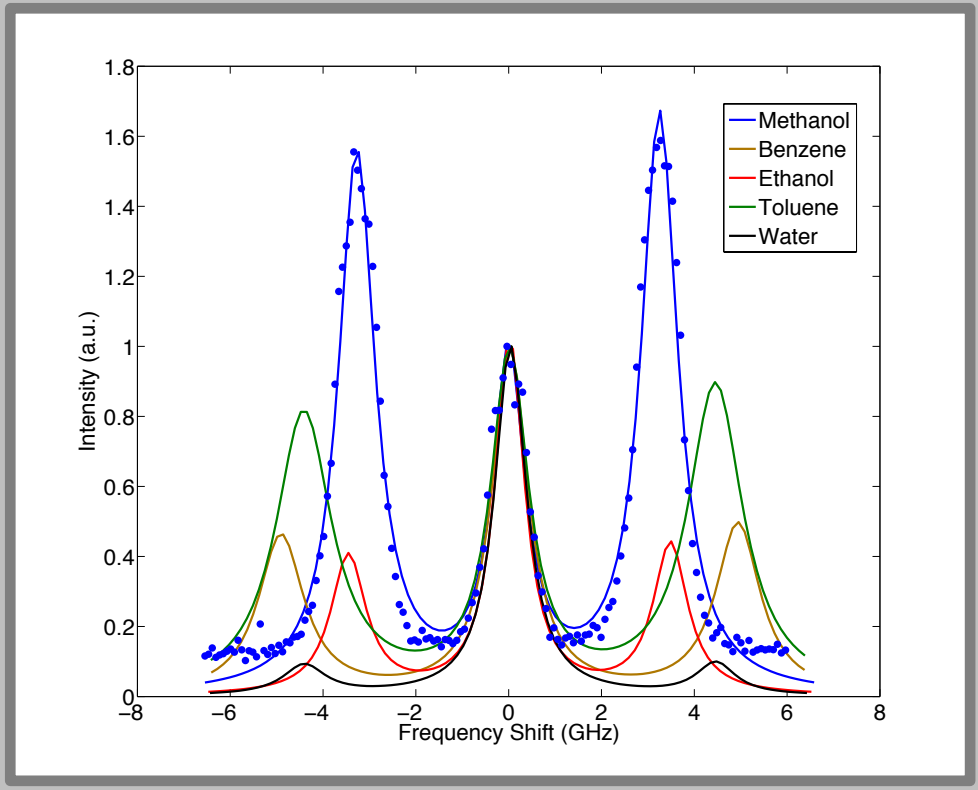
$$\omega(q) \equiv c_S q$$

$$c_S = \sqrt{\frac{E(1-\sigma)}{\varrho(1+\sigma)(1-2\sigma)}} = \sqrt{\frac{\lambda + 2\mu}{\varrho}} = \sqrt{\frac{M}{\varrho}}$$

$$\Gamma \equiv \tfrac{1}{2}[(\gamma - 1)D_T + D_V] = \tfrac{1}{2}\left[\frac{(\gamma - 1)\lambda}{m\rho_0 c_P} + \frac{\left(\eta_v + \frac{4}{3}\eta_s\right)}{m\rho_0} \right]$$

Formal results

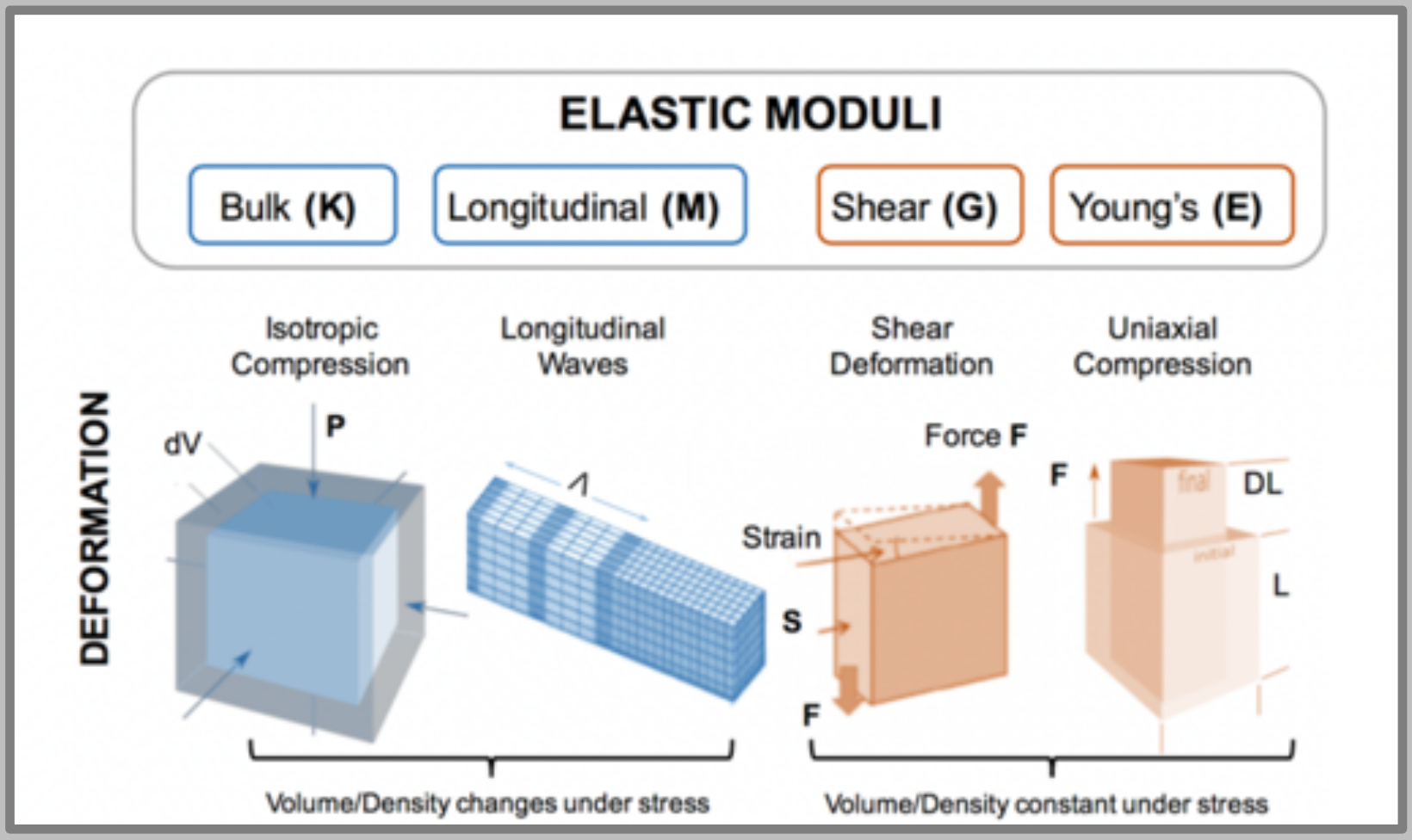
Brillouin microscopy



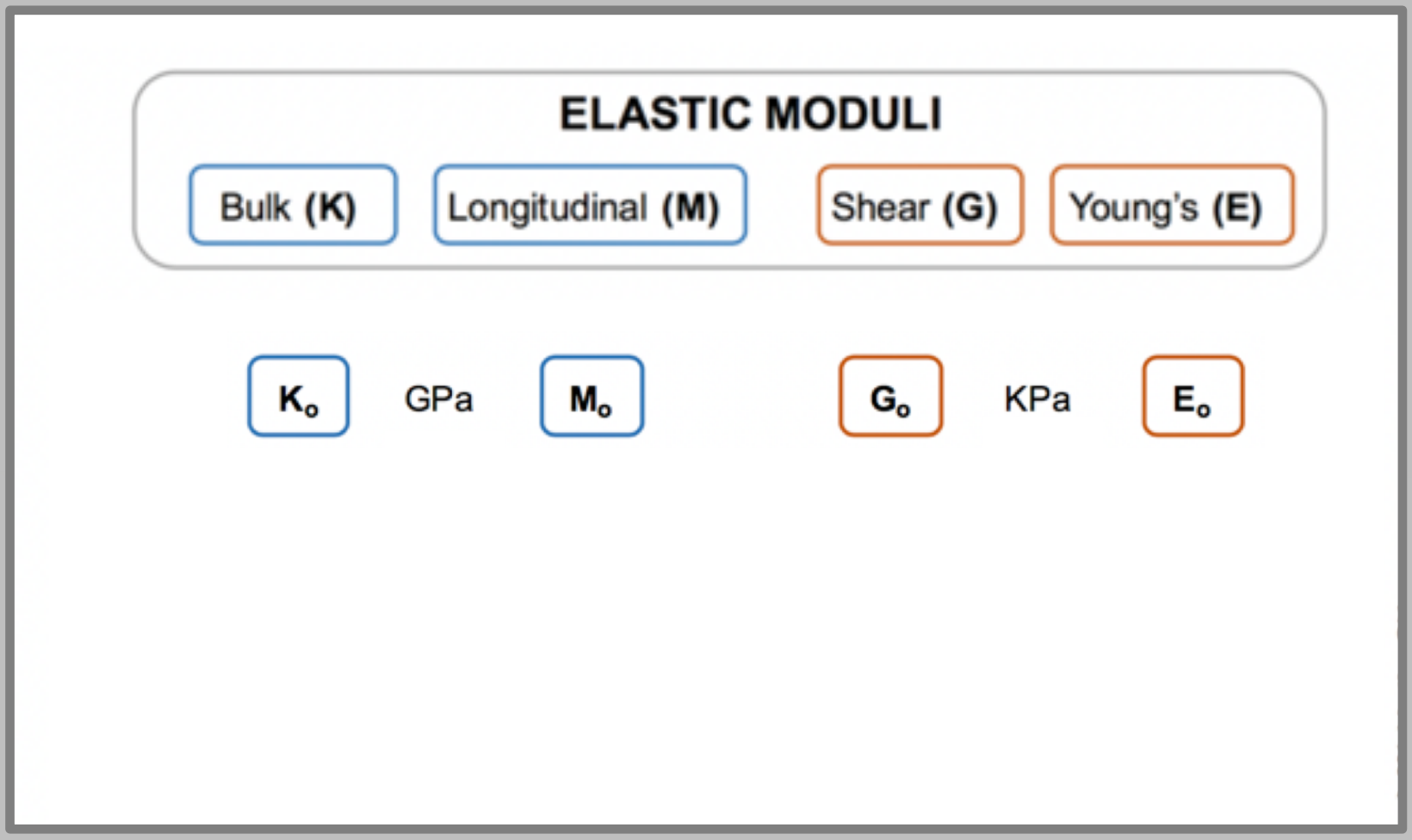
	ν_B (GHz) exp.	ν_B (GHz) theo.	V_{sound} (m/s)
Methanol	3.26±0.06	3.39	973.8
Benzene	4.92±0.07	4.38	1301.1
Ethanol	3.47±0.04	3.48	1012.1
Toluene	4.43±0.07	4.26	1174.7
Water	4.43±0.08	4.41	1341.5

- 0.1 sec exposure
- 5 mW at sample
- Low NA lens

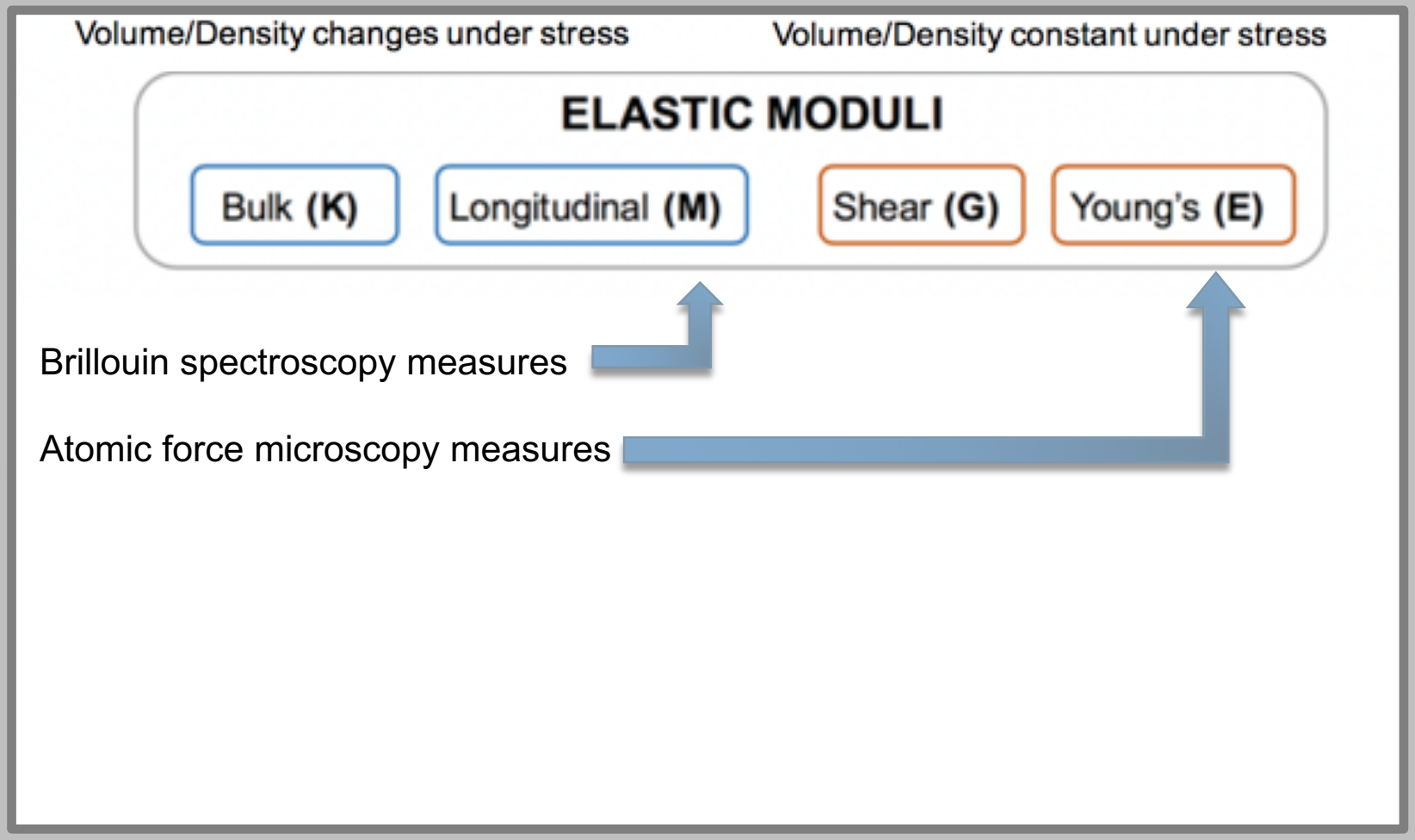
Examples



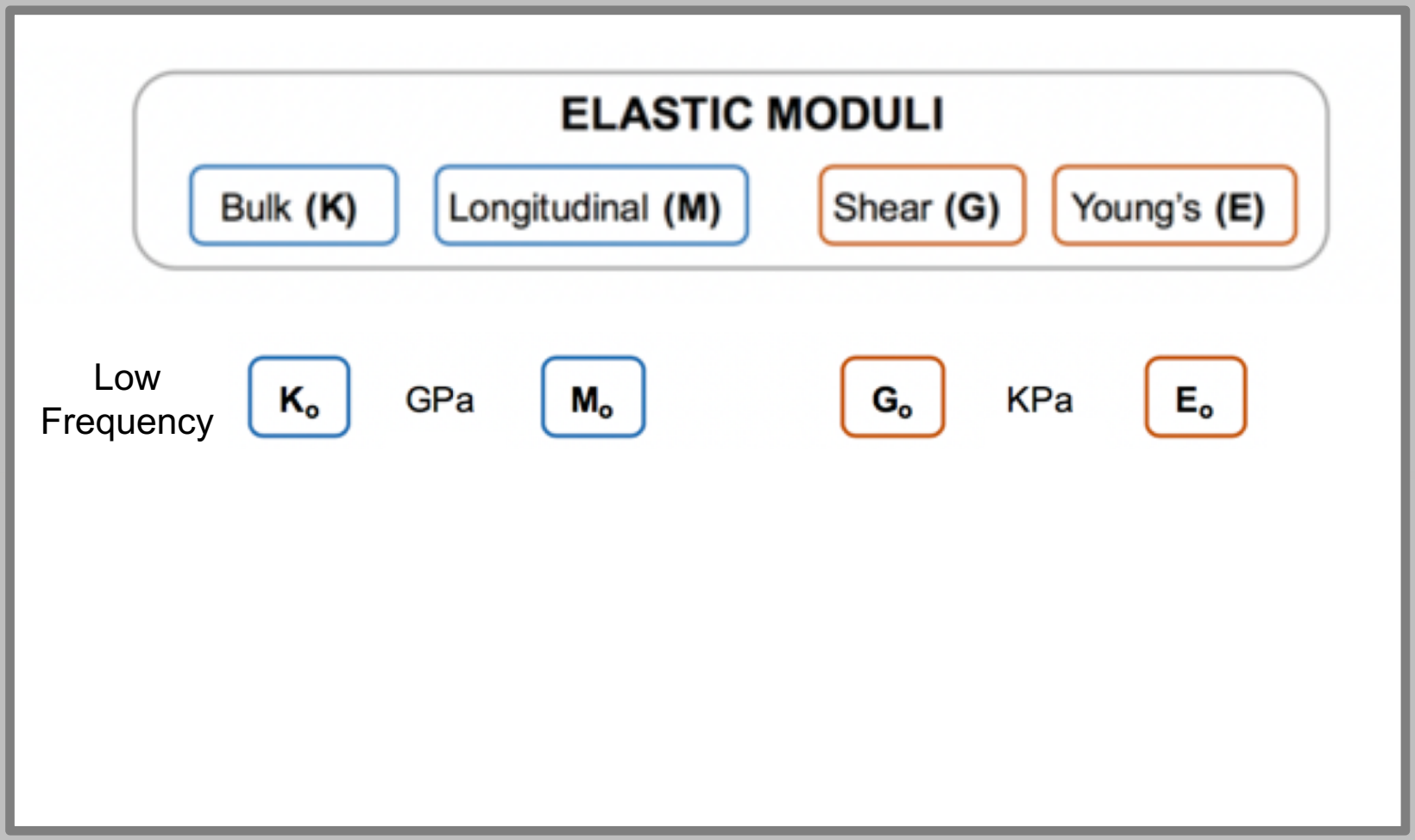
Elastic moduli



Elastic moduli



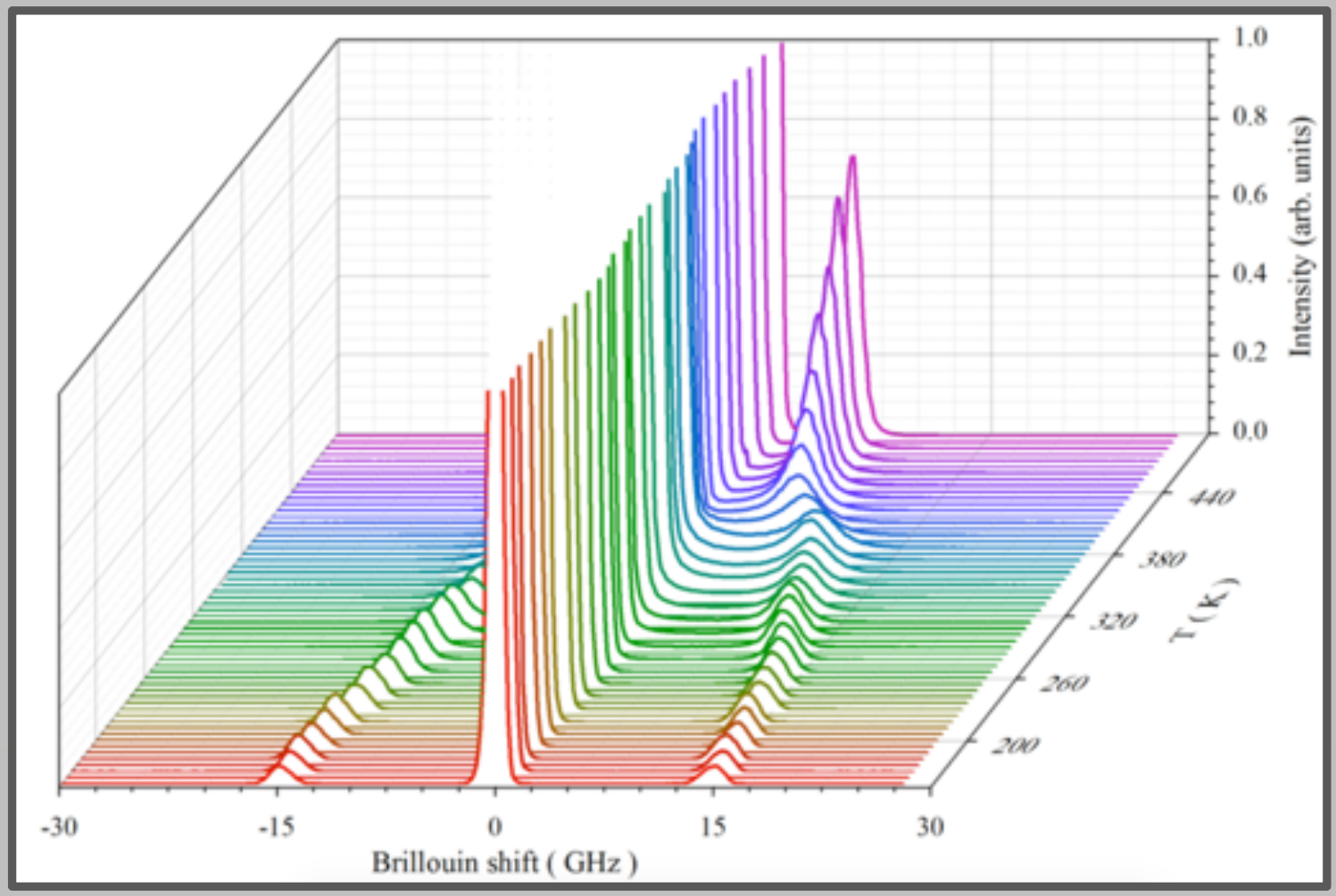
Elastic moduli



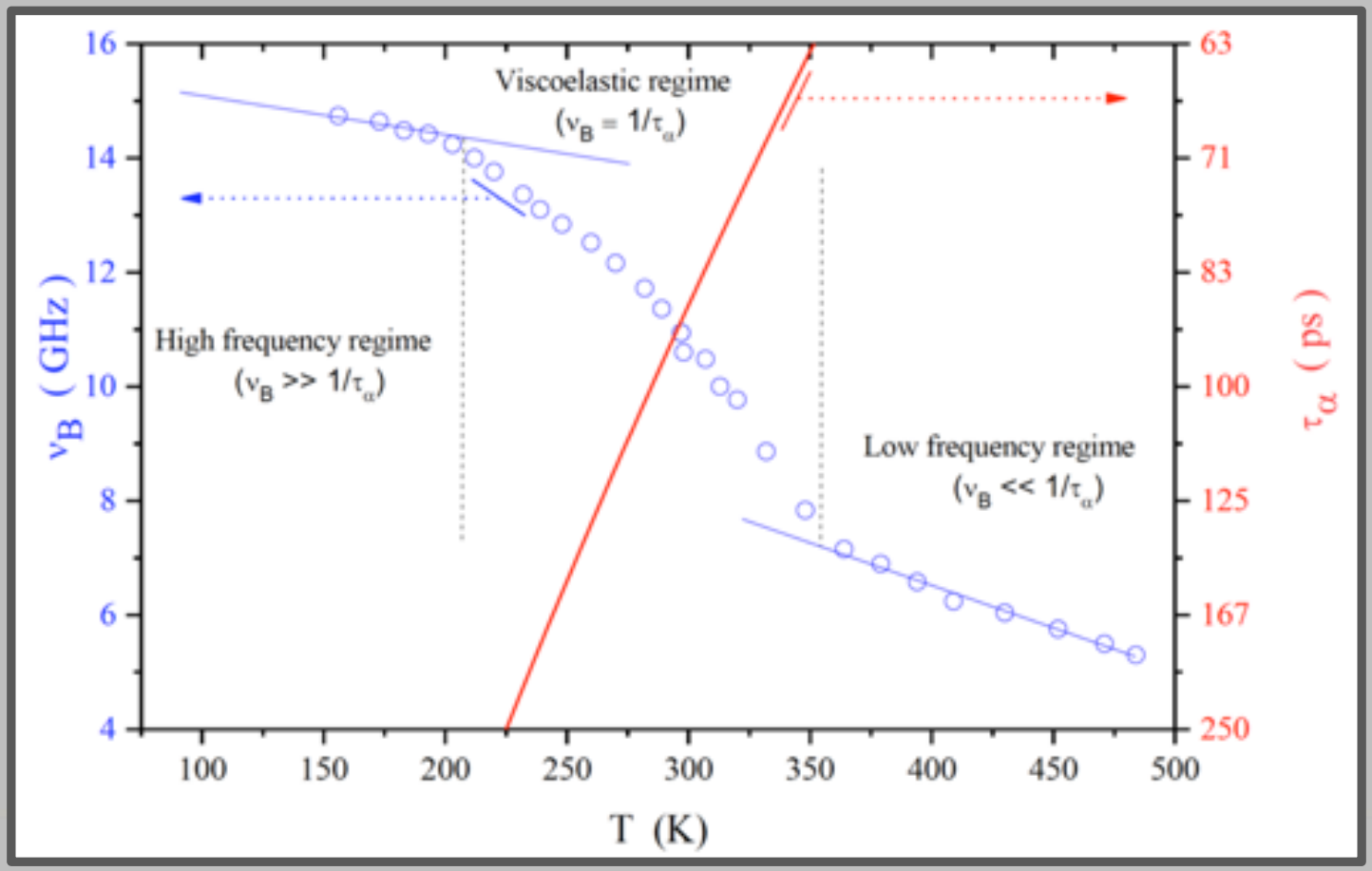
Elastic moduli

Viscoelasticity

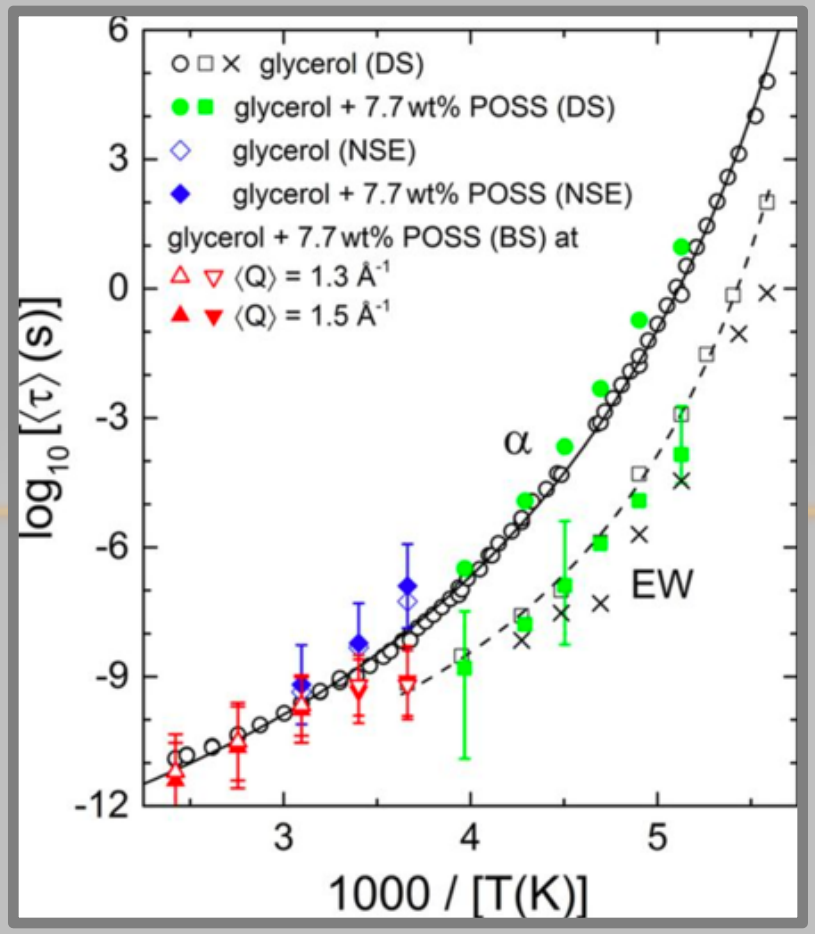
Liquid/glass glycerol – λ_o=514 nm – CW laser – 4 gratings monochromator



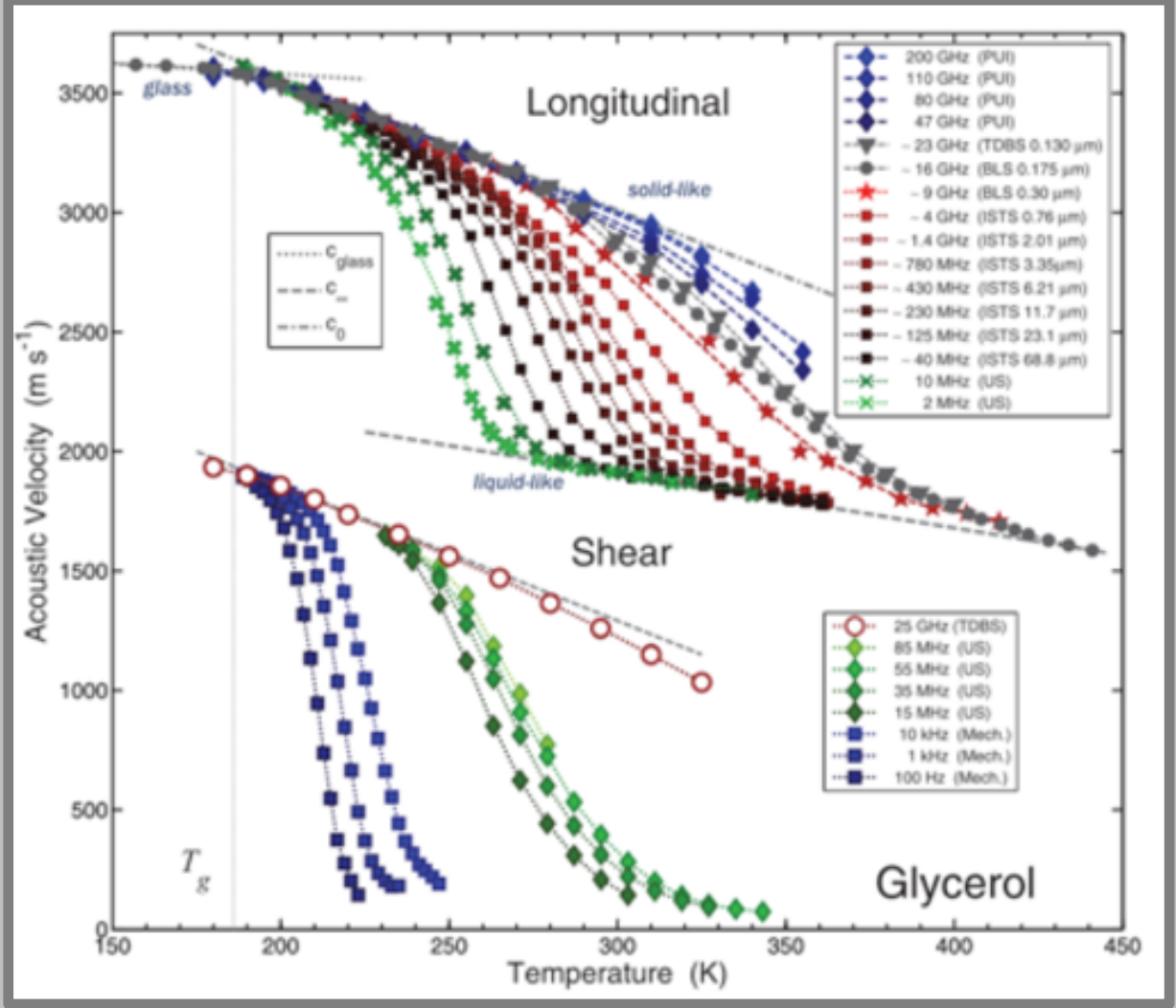
Viscoelasticity



Viscoelasticity



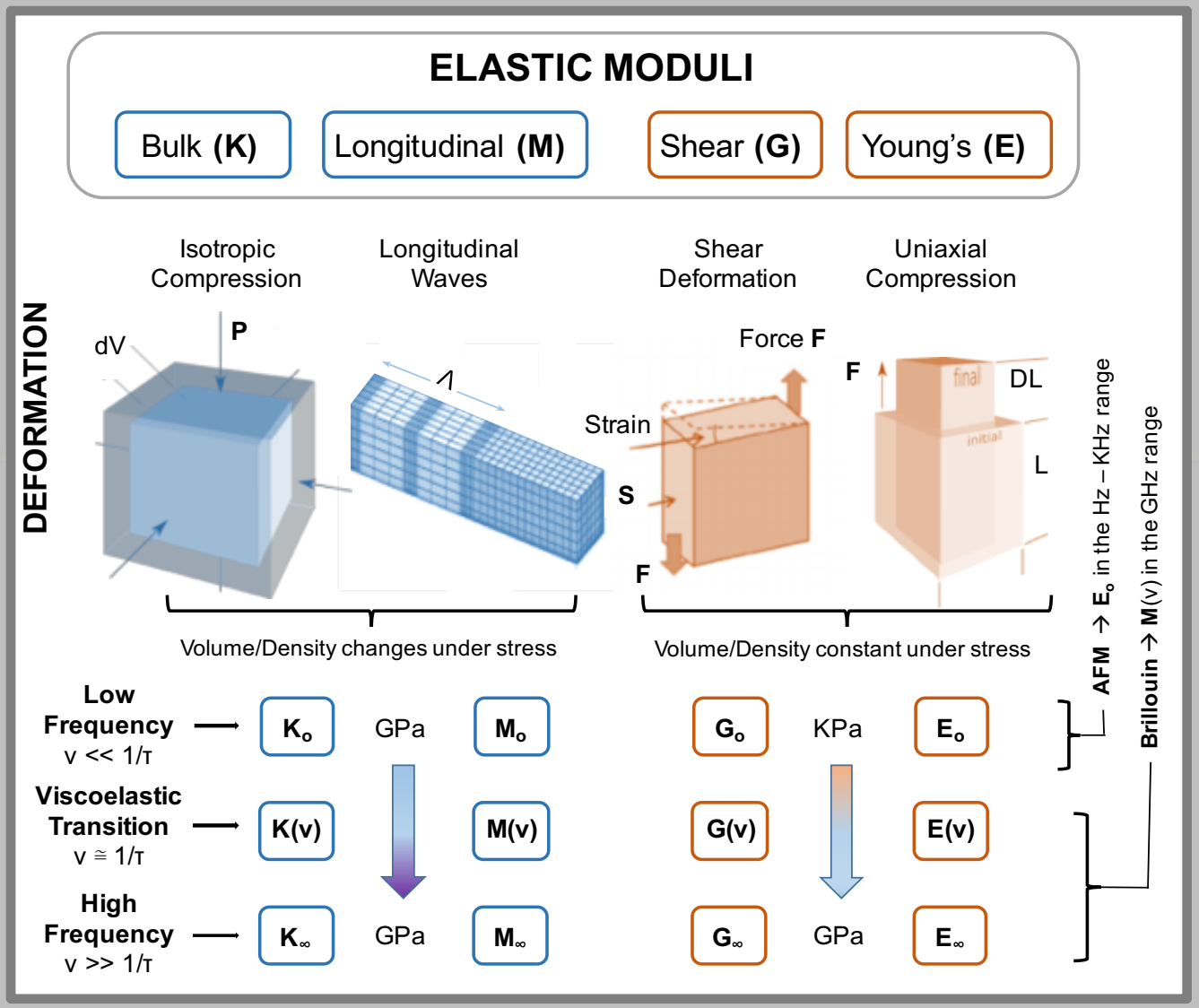
Viscoelasticity




THE JOURNAL OF CHEMICAL PHYSICS 138, 12A544 (2013)

Mechanical spectra of glass-forming liquids. II. Gigahertz-frequency longitudinal and shear acoustic dynamics in glycerol and DC704 studied by time-domain Brillouin scattering

Christoph Klieber,[1,a)] Tina Hecksher,[2,b)] Thomas Pezeril,[3] Darius H. Torchinsky,[4]


ELASTIC MODULI
Bulk (K)
Longitudinal (M)
Shear (G)
Young's (E)
DEFORMATION
Isotropic Compression
Longitudinal Waves
Shear Deformation
Uniaxial Compression
dV
P
Force F
Strain
S
F
final
initial
DL
L
Volume/Density changes under stress
Volume/Density constant under stress
Low Frequency
v << 1/τ
Viscoelastic Transition
v ≅ 1/τ
High Frequency
v >> 1/τ
K₀
K(v)
K∞
GPa
M₀
M(v)
M∞
G₀
G(v)
G∞
KPa
GPa
E₀
E(v)
E∞
AFM → E₀ in the Hz – KHz range
Brillouin → M(v) in the GHz range

First imaging

APPLIED PHYSICS LETTERS 87, 061903 (2005)

Brillouin imaging

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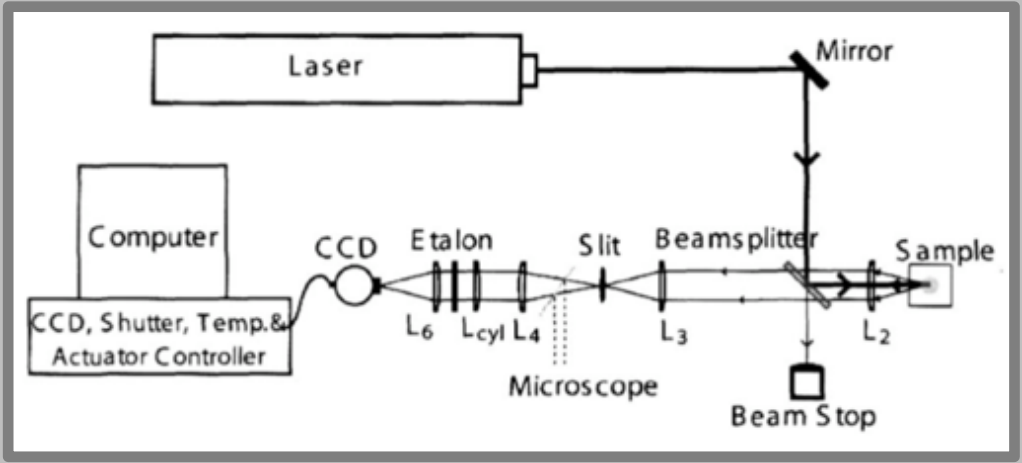
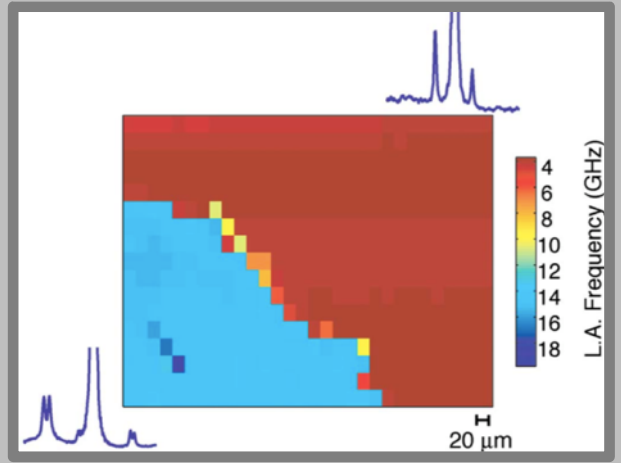
Department of Chemistry and Biochemistry, Arizona State University, Tempe, Arizona 85287

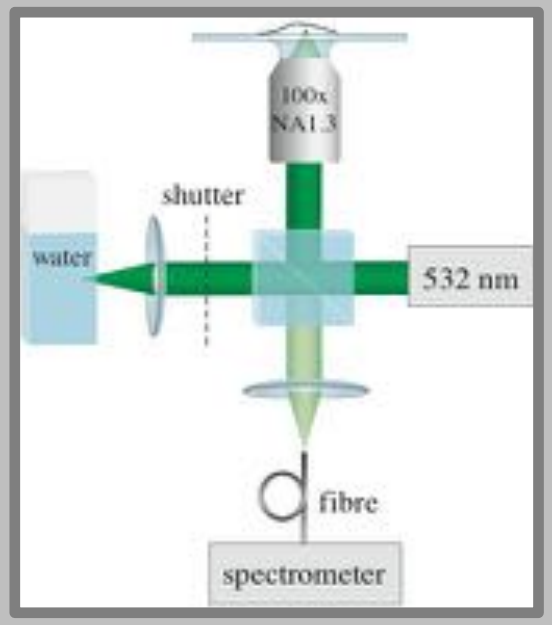
(Received 7 April 2005; accepted 16 June 2005; published online 1 August 2005)

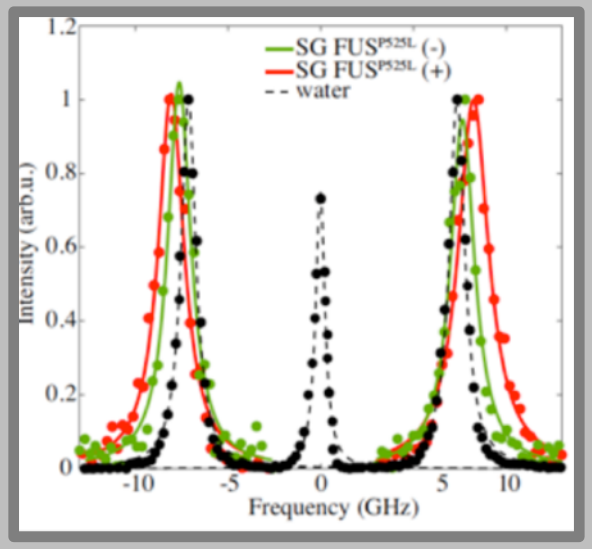
Using an angle-dispersive Fabry-Perot interferometer in a confocal backscattering geometry, we have obtained Brillouin images of several liquid and polymer materials. One- and two-dimensional images of heterogeneous samples are presented using longitudinal Brillouin frequency shifts and acoustic attenuation for contrast. The experimental resolution of the images is 20 μm. © *2005 American Institute of Physics*. [DOI: 10.1063/1.1999857]

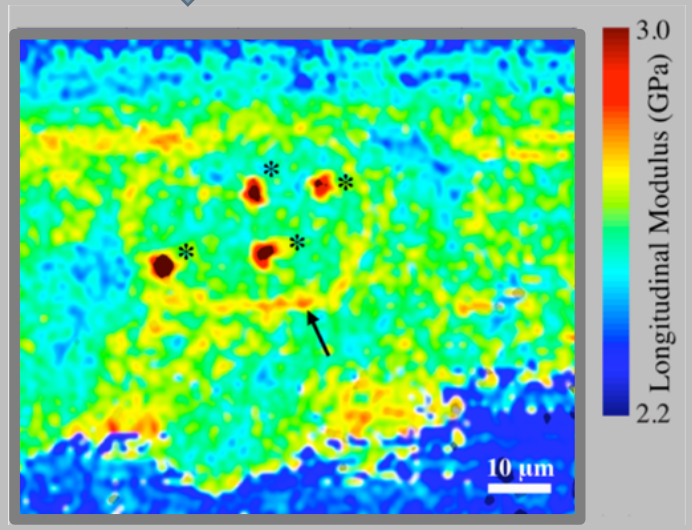




Concept







Spatial resolution

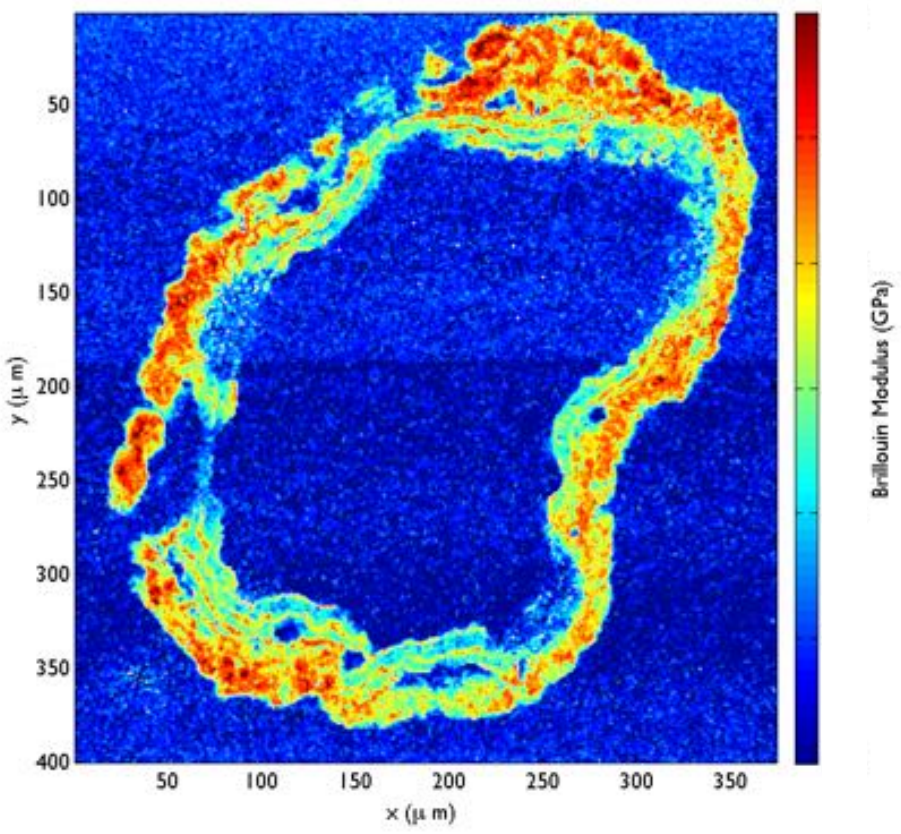
$r \simeq 0.3\mu m \quad z \simeq 1\mu m$

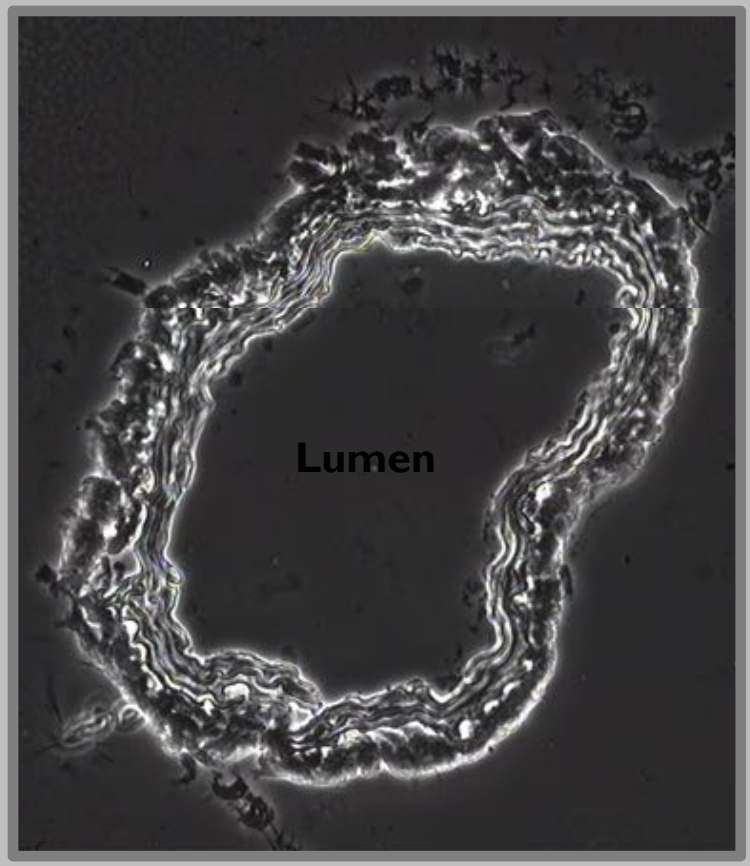
- 10 mW at sample
- 0.1 sec / spectrum

Towards BLS microscopy

Applications#1 Tissues

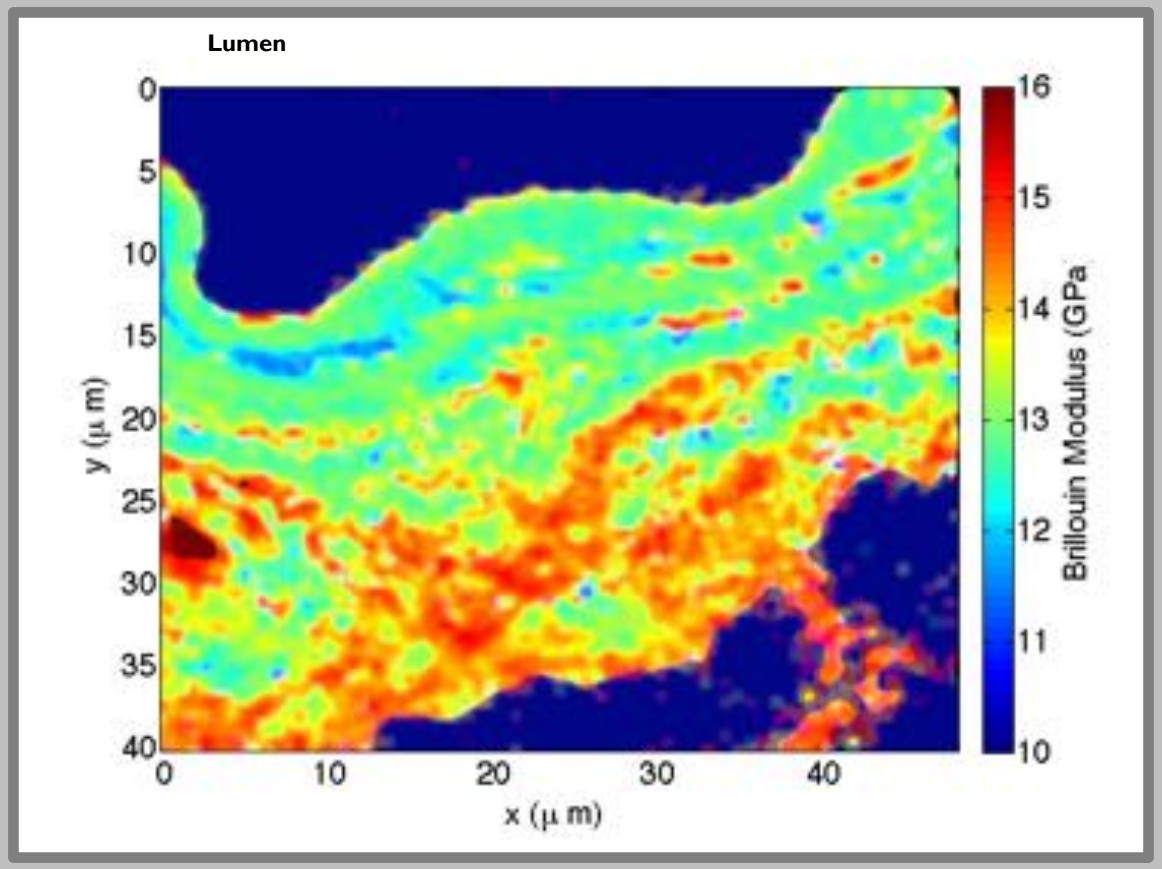
Healthy Blood Vessel



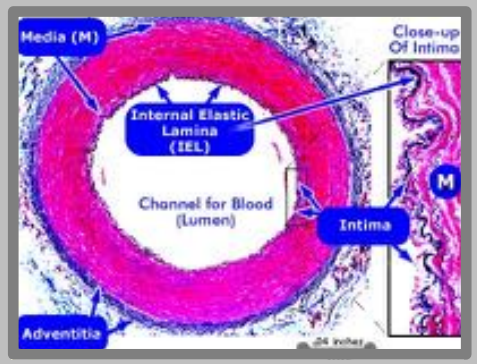


Towards BLS microscopy

Applications#1 Tissues



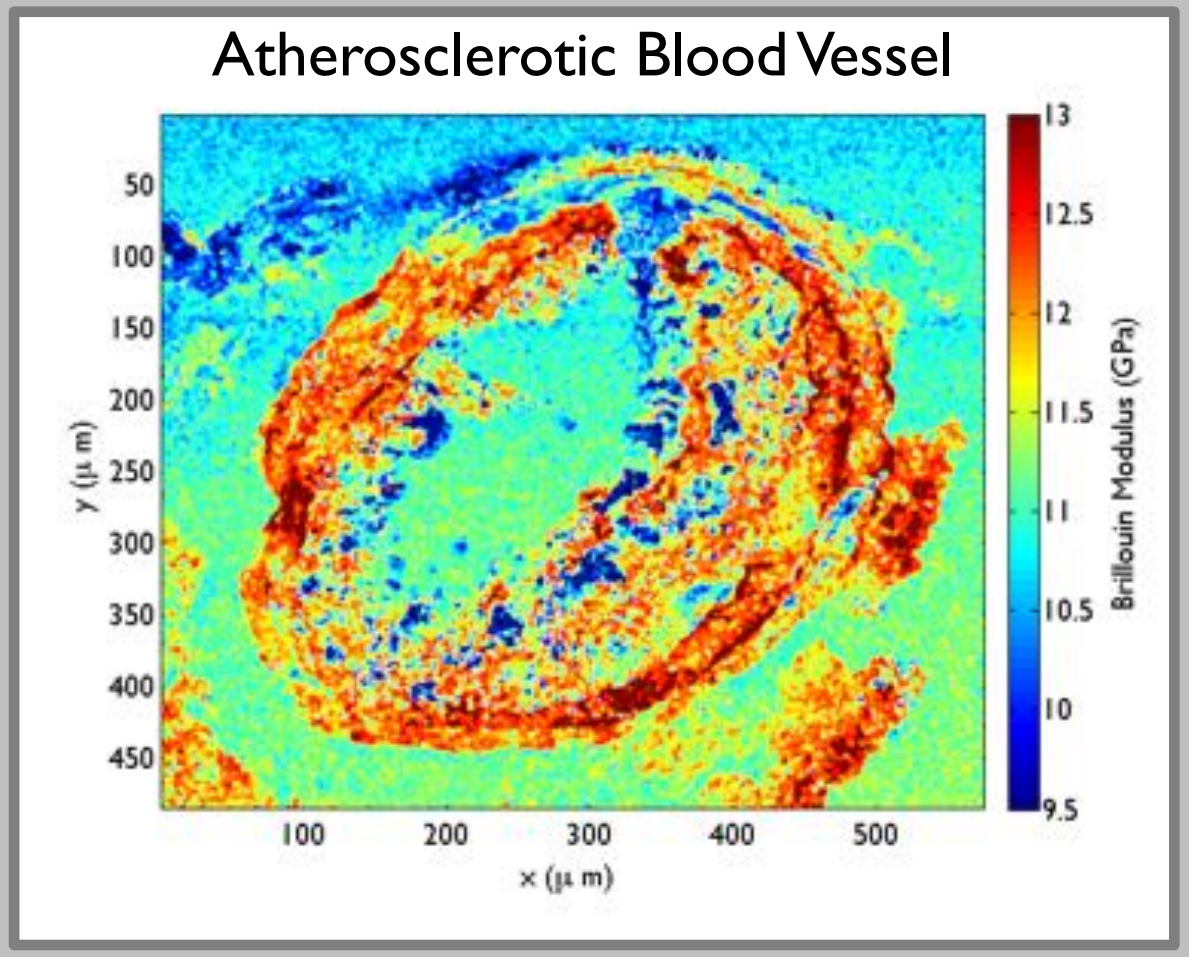
- Artery Cross Section



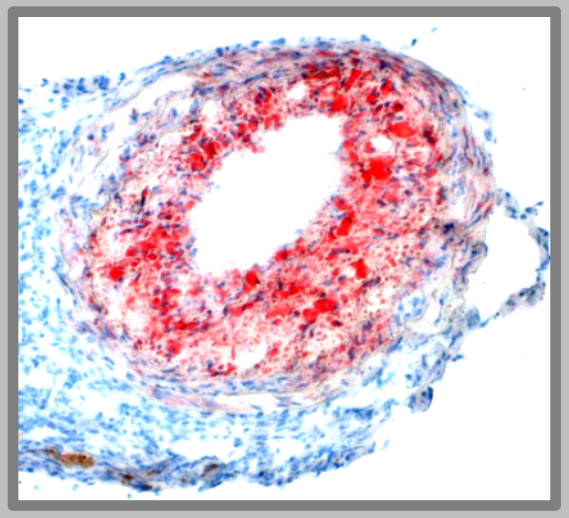
Elasticity difference in structural layers can be a fingerprint for *Atherosclerosis*

Towards BLS microscopy

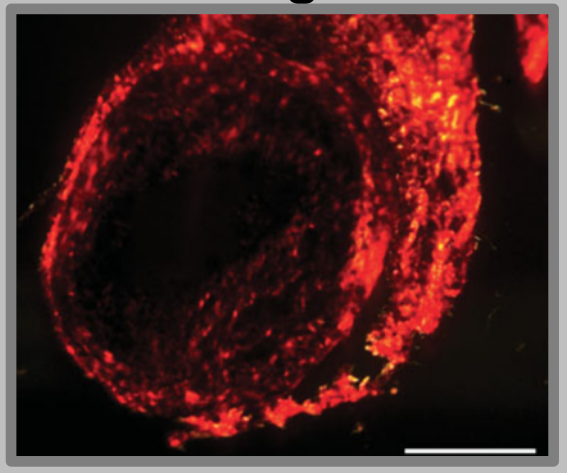
Applications#1 Tissues



lipid



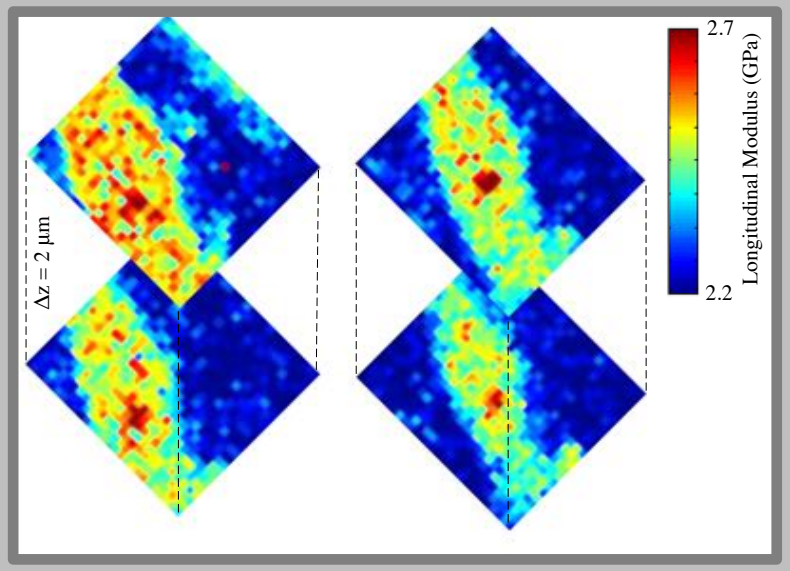
collagen

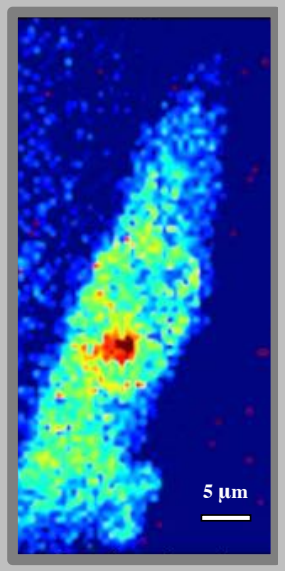


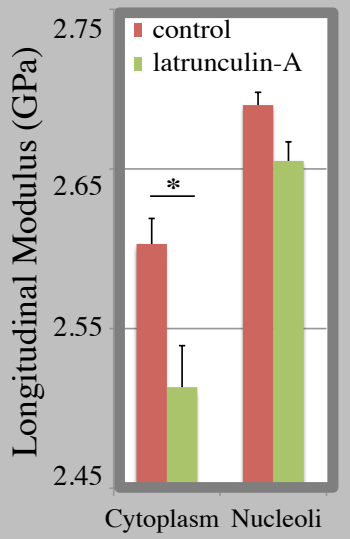
G. Antonacci et al. "Quantification of plaque stiffness by Brillouin Microscopy in experimental thin cap fibroatheroma". *J R Soc Interface.*, **12(112),** 2015

Towards BLS microscopy

Applications#2 Cells





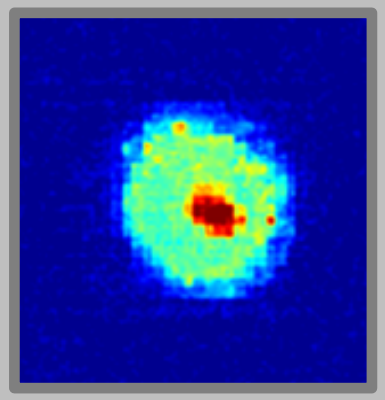


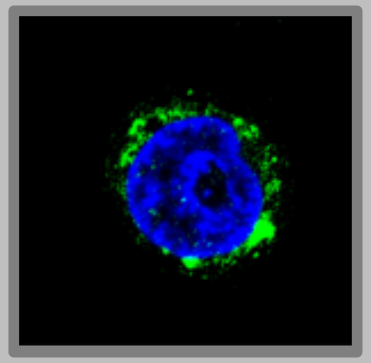
- **Tracking variations in cellular stiffness in response to external stimuli**
  - Cellular stiffness decreased significantly after exposure to Lactrunculin-A

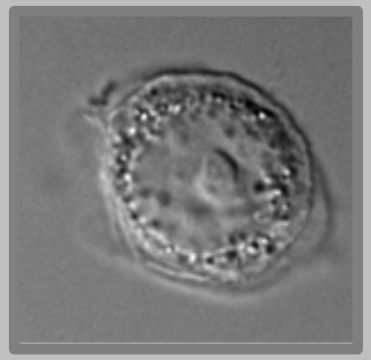
Towards BLS microscopy

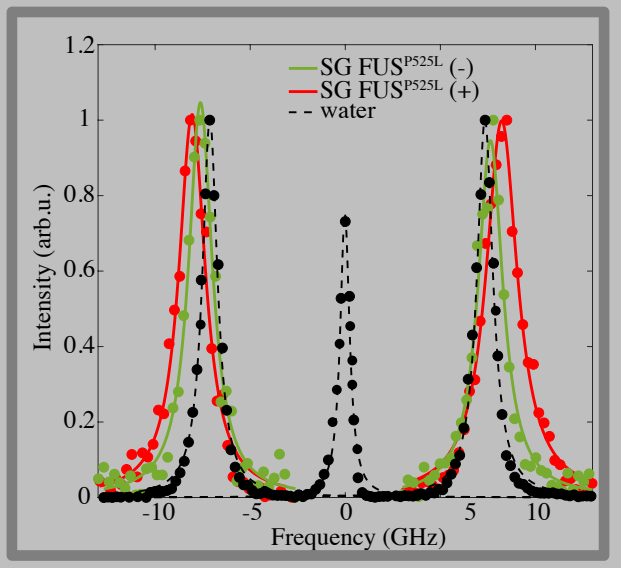
Applications#3 Cells

FUS (-)

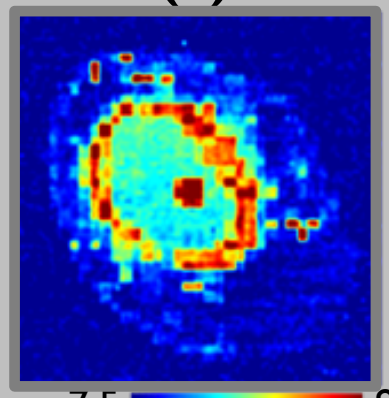


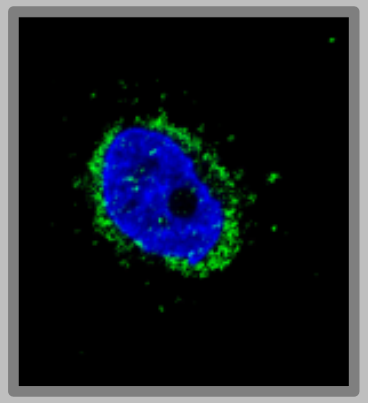


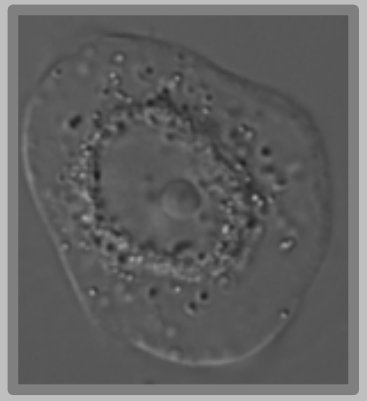




FUS (+)







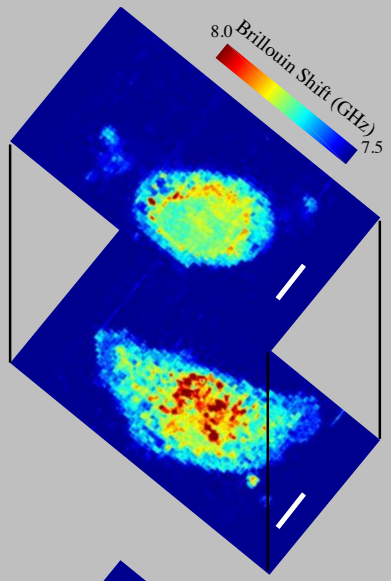
7.5 8.0
Brillouin Shift (GHz)

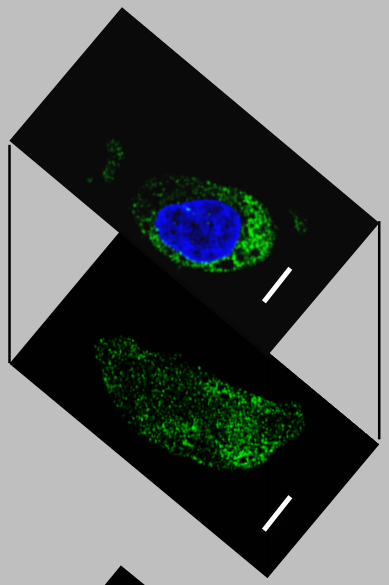
- A liquid-solid phase transition occurs in the presence of ALS-linked FUS protein

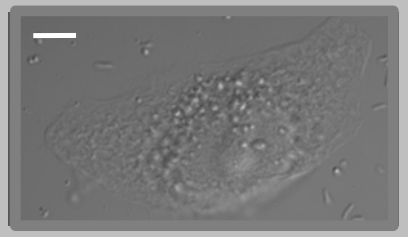
Towards BLS microscopy

Applications#3 Cells

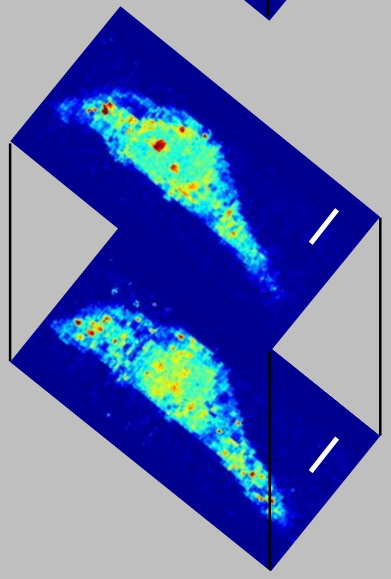
FUS (-)

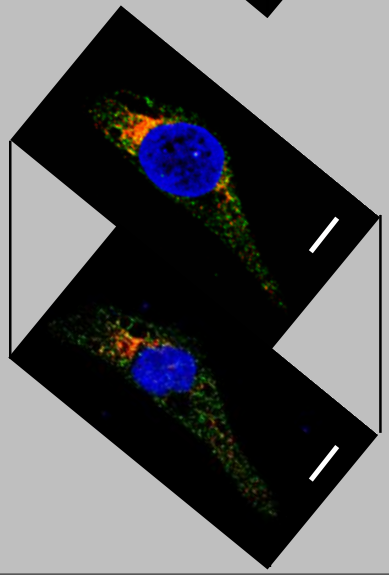


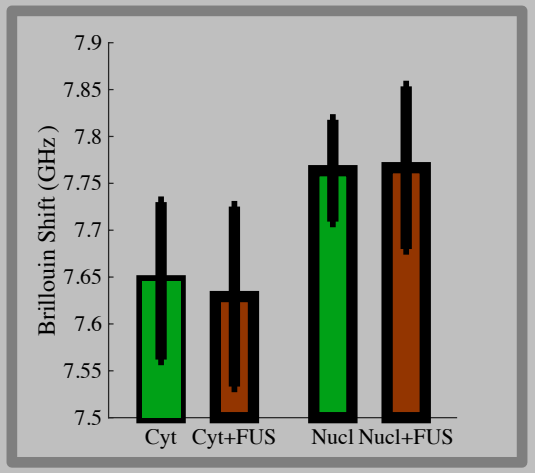


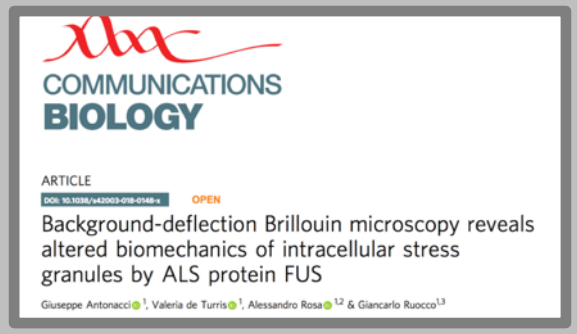


FUS (+)



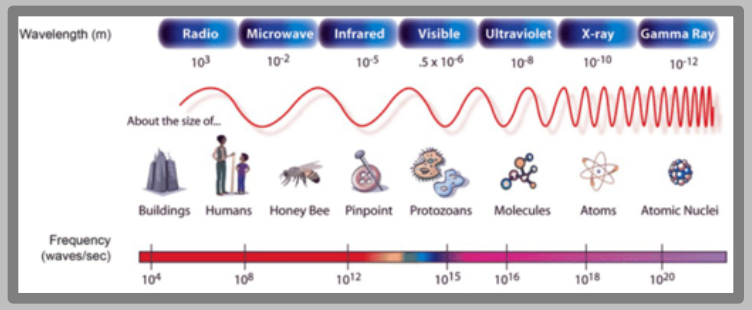


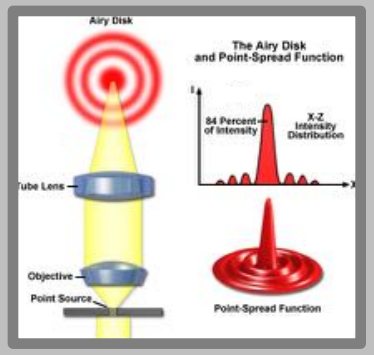


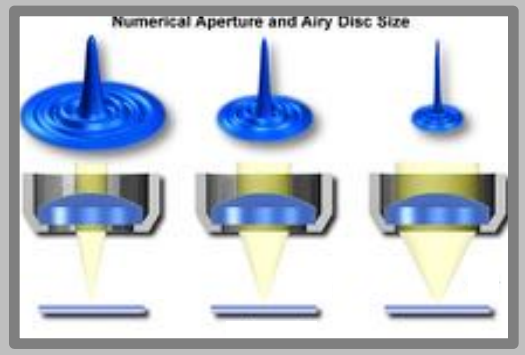


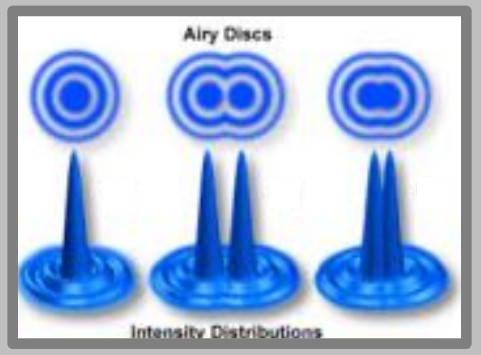
4. Scattering Assisted Microscopy (SAM)

Resolution : what can we "see" ?



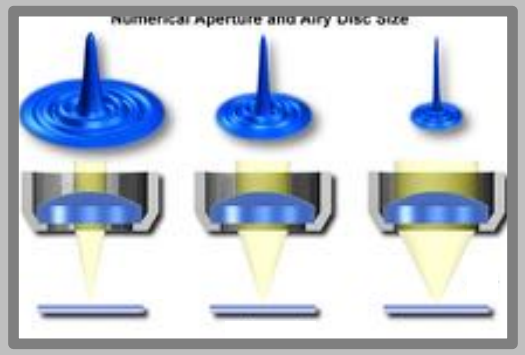






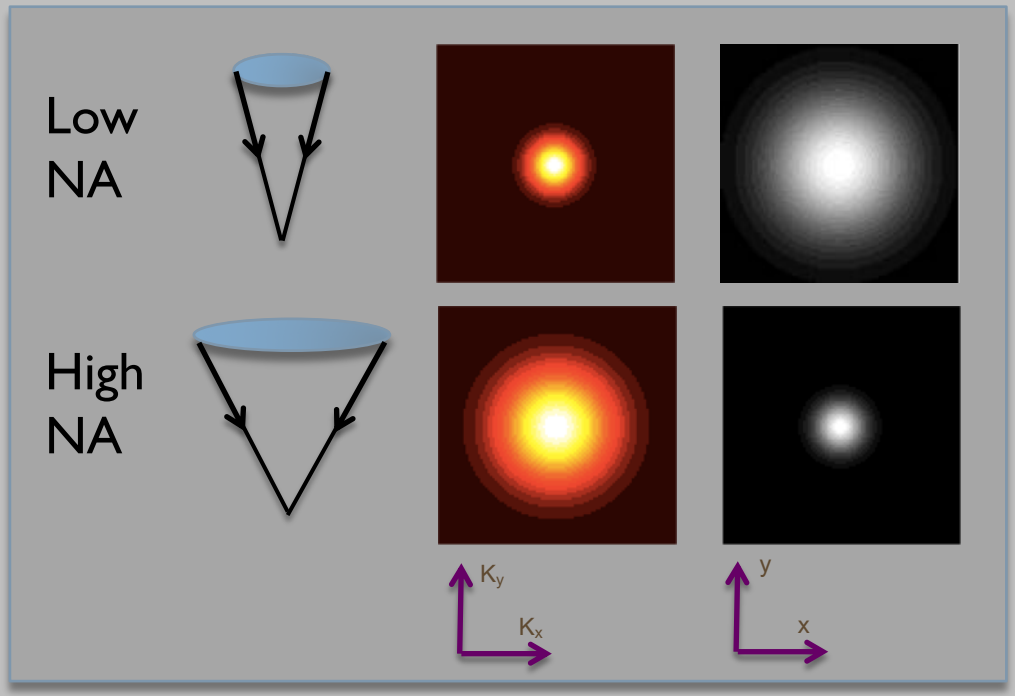
Resolution vs NA

Numerical aperture and spatial resolution



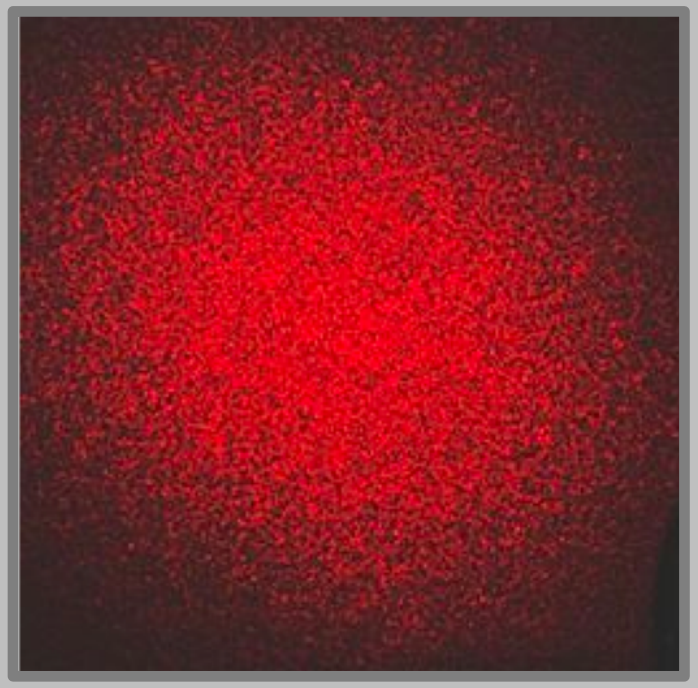
$\Delta x = l / 2 n NA$

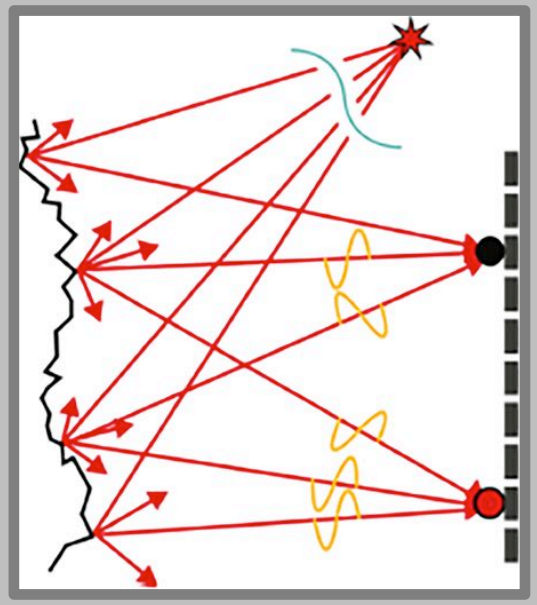
Microscopy guys jargon



NA ⟷ working distance

Speckles field

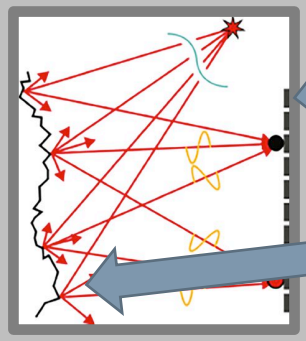


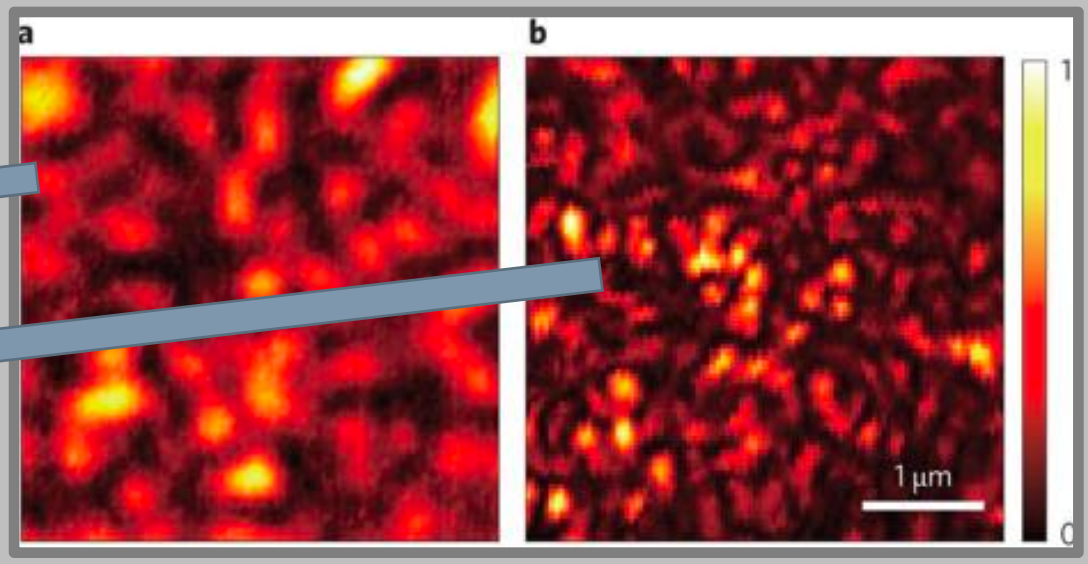


Speckles field

(a) Far field

- Diffraction limited





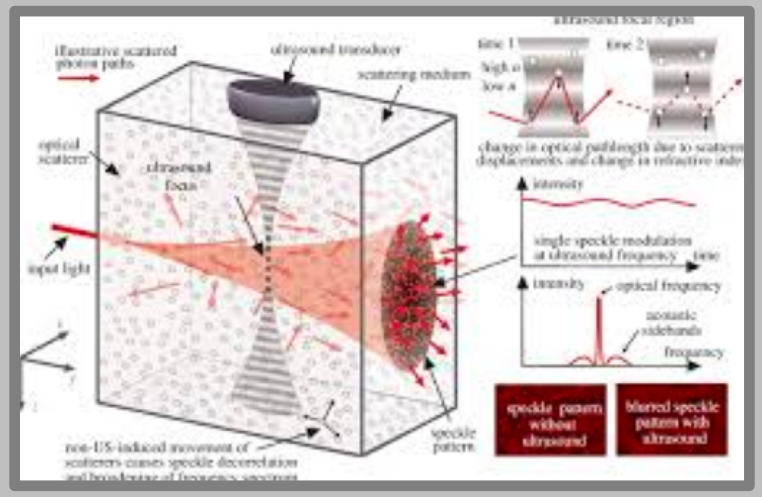
(b) Near field

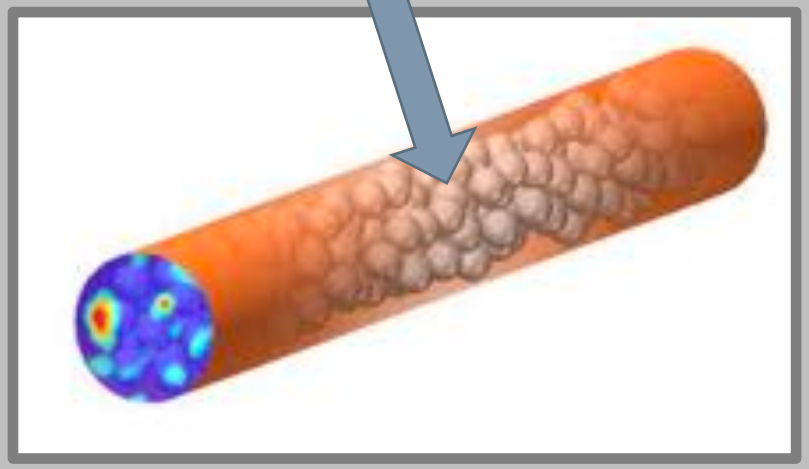
- Sub-diffraction
- Measured by SNOM
- ..NA .. π

$$P(\xi) = \Gamma \exp(-\Gamma\xi)$$

Speckles field

What about "inside" the scatterers ?

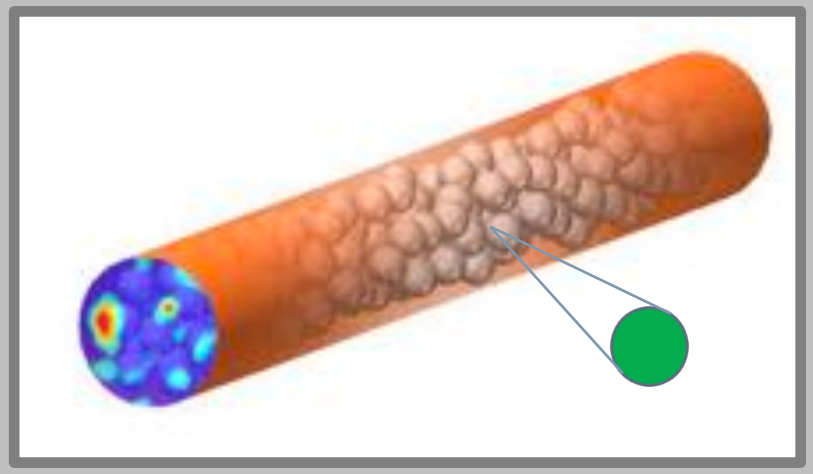




NA ... 4π

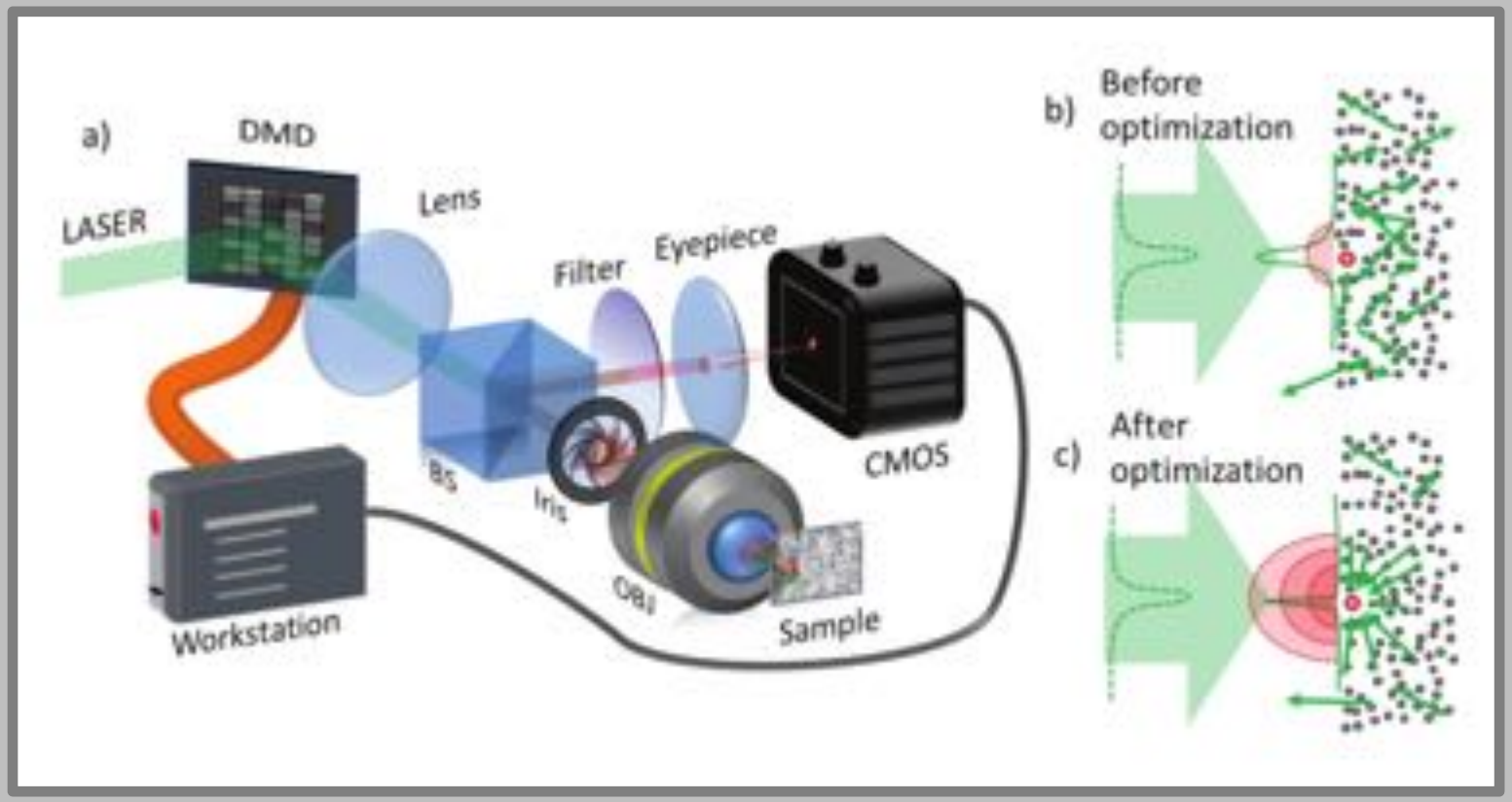
Scattering assisted microscopy

Super-resolution?

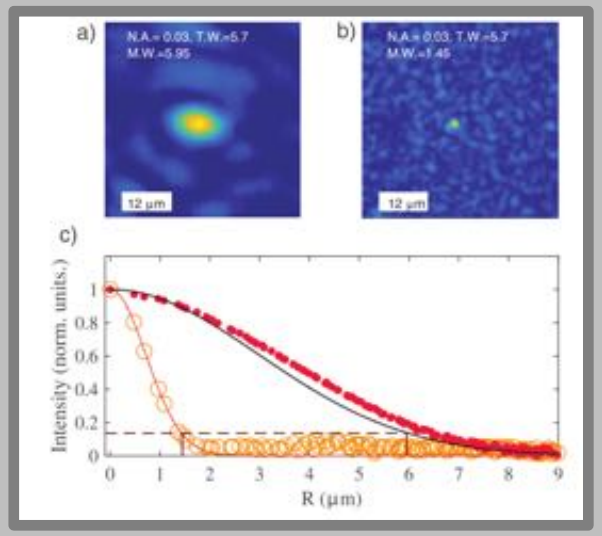


Fluorescent bead/molecule

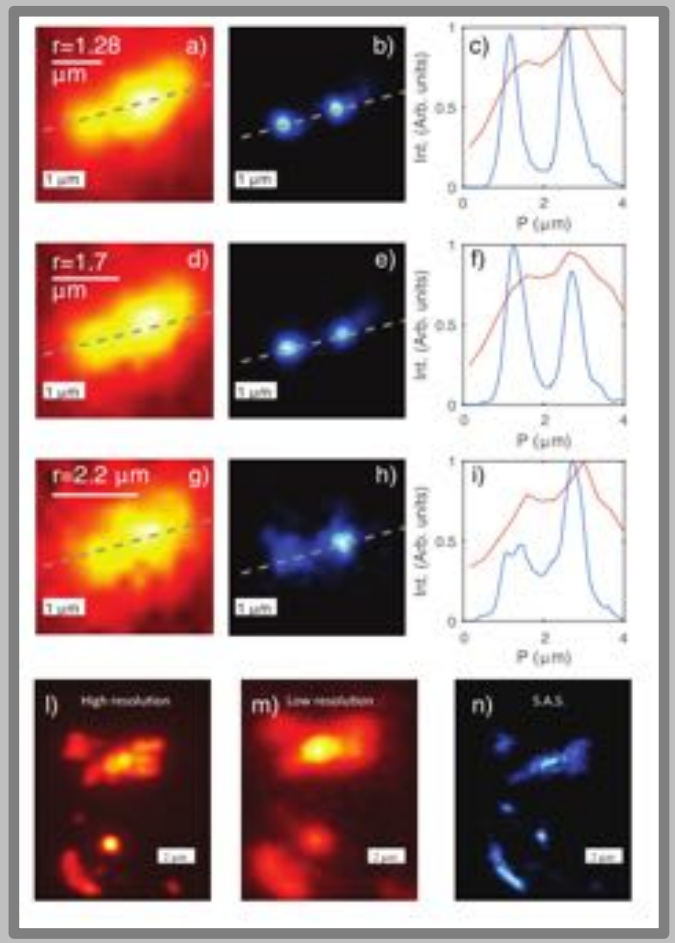
Scattering assisted microscopy



Scattering assisted microscopy



More important ....
Long Working Distance



SCIENTIFIC REPORTS

OPEN

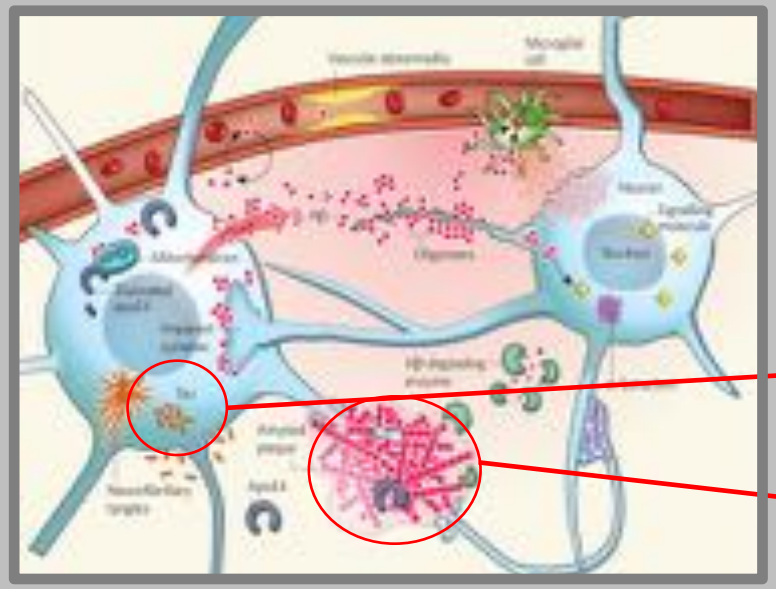
Scattering Assisted Imaging

Marco Leonetti[1,2], Alfonso Grimaldi[1], Silvia Ghirga[1,3], Giancarlo Ruocco[1,3] & Giuseppe Antonacci[3,4]

SAM : applications

Basically: taking advantage of the disorder of the sample allow us to emulate "large angles" having the objective far away from the sample:
submicron resolution at tens of millimeters distance

Application: Early diagnosis of Alzheimer Disease (AD)



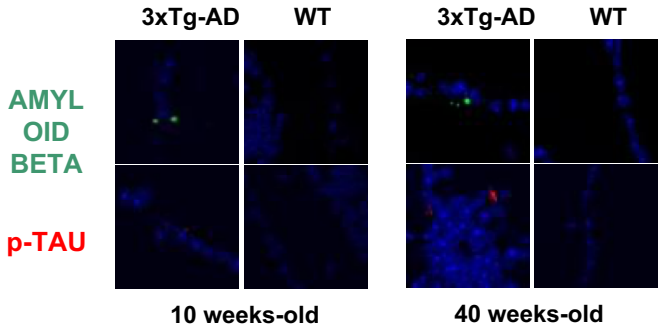
AD ⟺ β-Amyloid + TAU aggregates

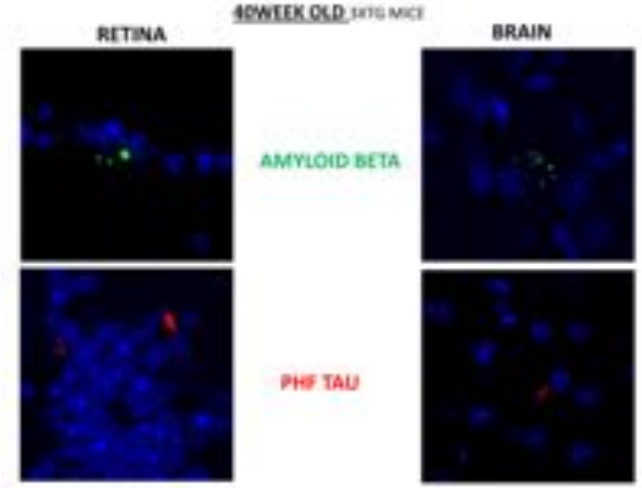
TAU intracellular aggregates

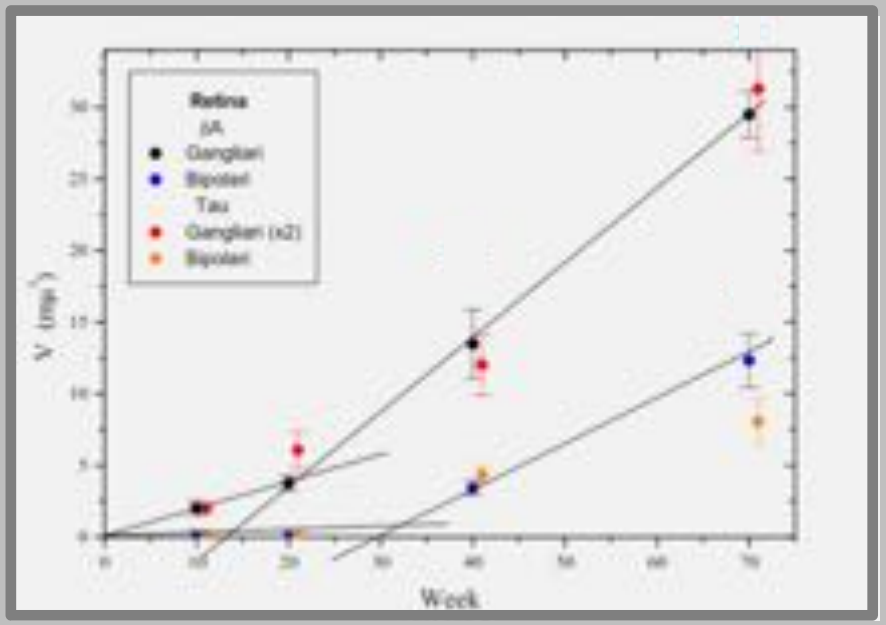
β-Amyloid extracellular aggregates

Early detection of AD : Mouse model

Retinal amyloid and tau plaques dimension
increases with age and **change localization**







Grimaldi et al. Cell Death and Disease (2018)9:685
DOI 10.1038/s41419-018-0740-5

Cell Death & Disease

ARTICLE Open Access

Inflammation, neurodegeneration and protein aggregation in the retina as ocular biomarkers for Alzheimer's disease in the 3xTg-AD mouse model

Alfonso Grimaldi[1], Carlo Brighi[1], Giovanna Peruzzi[1], Davide Ragozzino[2,3], Valentina Bonanni[4], Cristina Limatola[2,3], Giancarlo Ruocco[1,5] and Silvia Di Angelantonio[1,2]

Early detection of AD : Human post mortem

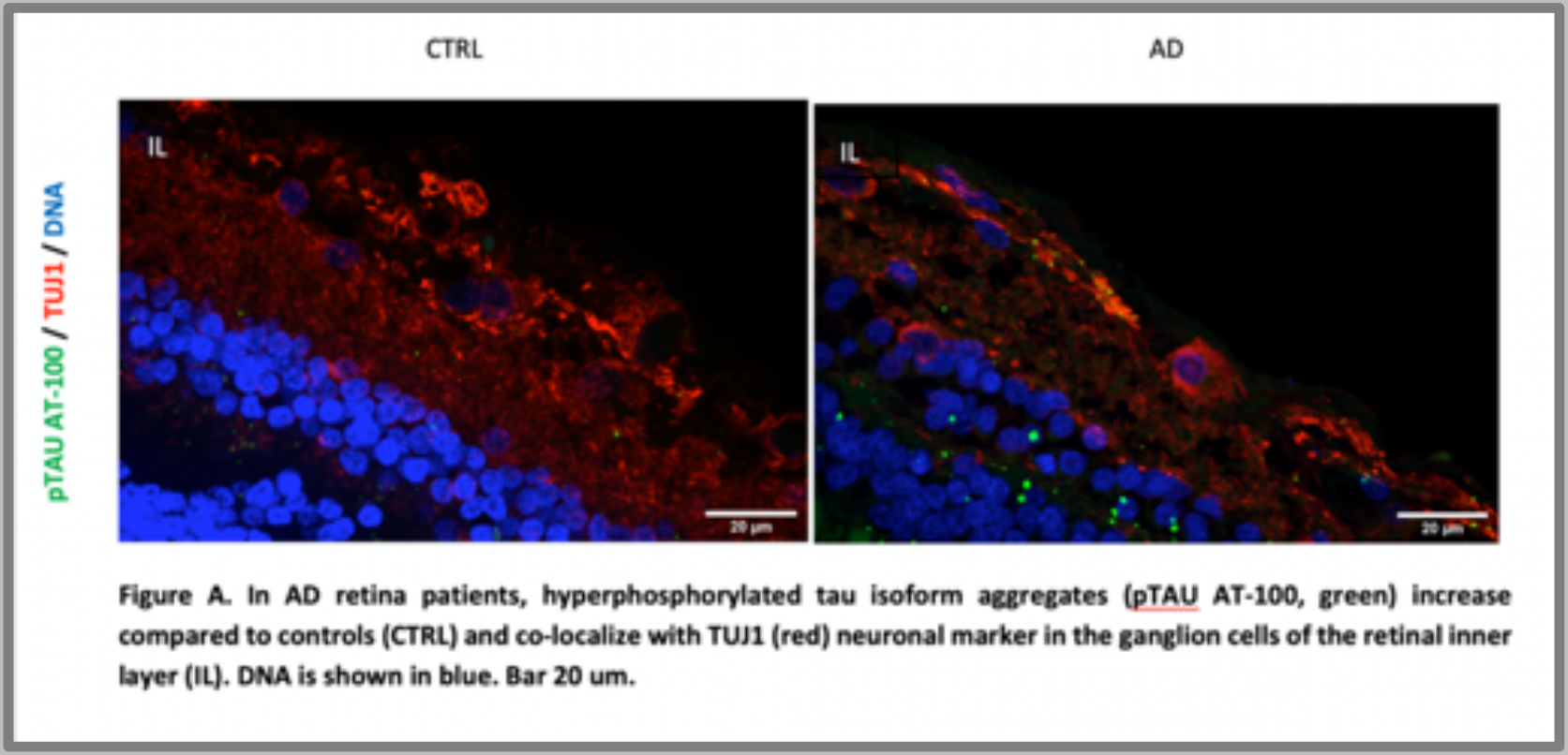
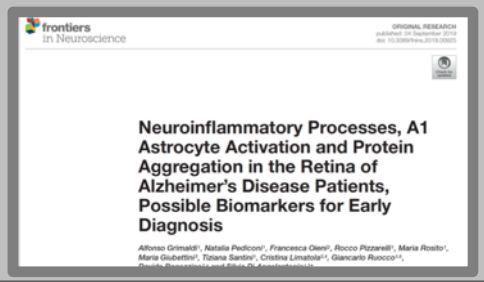


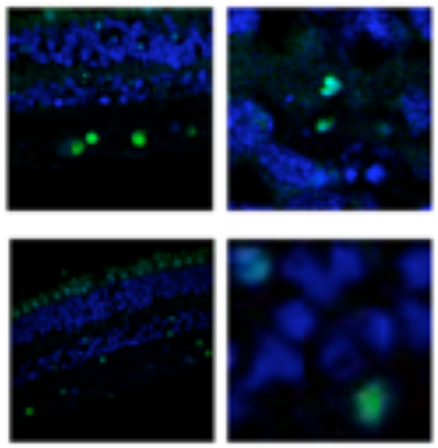
Figure A. In AD retina patients, hyperphosphorylated tau isoform aggregates (pTAU AT-100, green) increase compared to controls (CTRL) and co-localize with TUJ1 (red) neuronal marker in the ganglion cells of the retinal inner layer (IL). DNA is shown in blue. Bar 20 um.


frontiers in Neuroscience

ORIGINAL RESEARCH

Neuroinflammatory Processes, A1 Astrocyte Activation and Protein Aggregation in the Retina of Alzheimer's Disease Patients, Possible Biomarkers for Early Diagnosis

Early detection of AD : Human post mortem



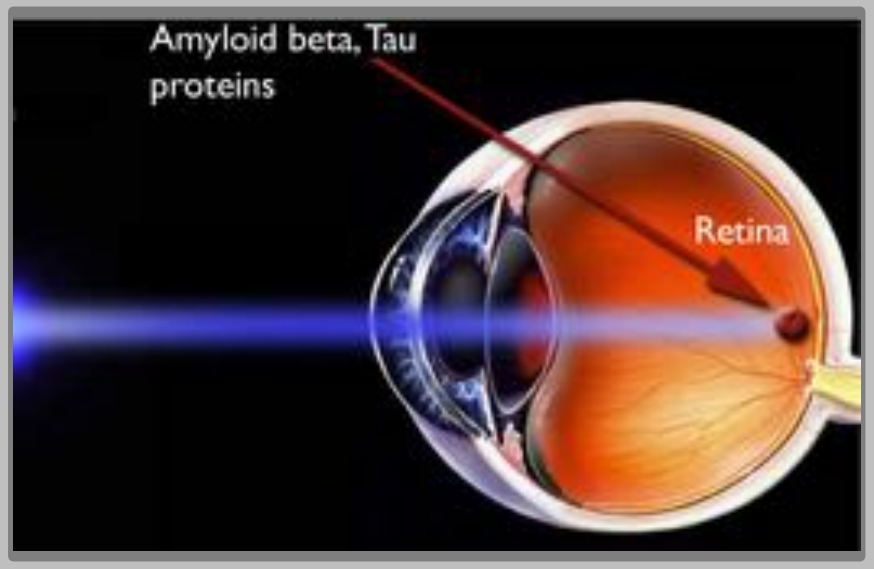
Representative images of human retinal slices from a AD patients and age-matched non AD control subjects (Eye bank at st. Michaels hospital, Canada) immunolabeled with Anti-TDP43 antibody (ab109535; green) and Hoechst for nuclei visualization (blue). Note that TDP43 is expressed only in the nucleus of retinal cells in control tissue while the cytoplasmic, pathological expression, was observed only in AD retinal slices.

Early detection of AD

Aggregation of Amyloid-β and TAU proteins, and the consequent loss of neurons functionality, starts around 10-15 years before manifestation of cognitive decline.

In the retinal tissue, which is part of the central nervous system, it has been demonstrated the presence of β-Amyloid plaques and accumulations of TAU protein in AD patients and in murine models of AD.

SAM allows for the in vivo detection of protein aggregation in the retina.



CLNS - Thanks

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3. New dimension in microscopy: imaging mechanical properties

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4. Diagnosis of Neurodegenerative Diseases (AD, PD, AMD, ALS, …) via newly developed HR/LWD imaging systems.

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