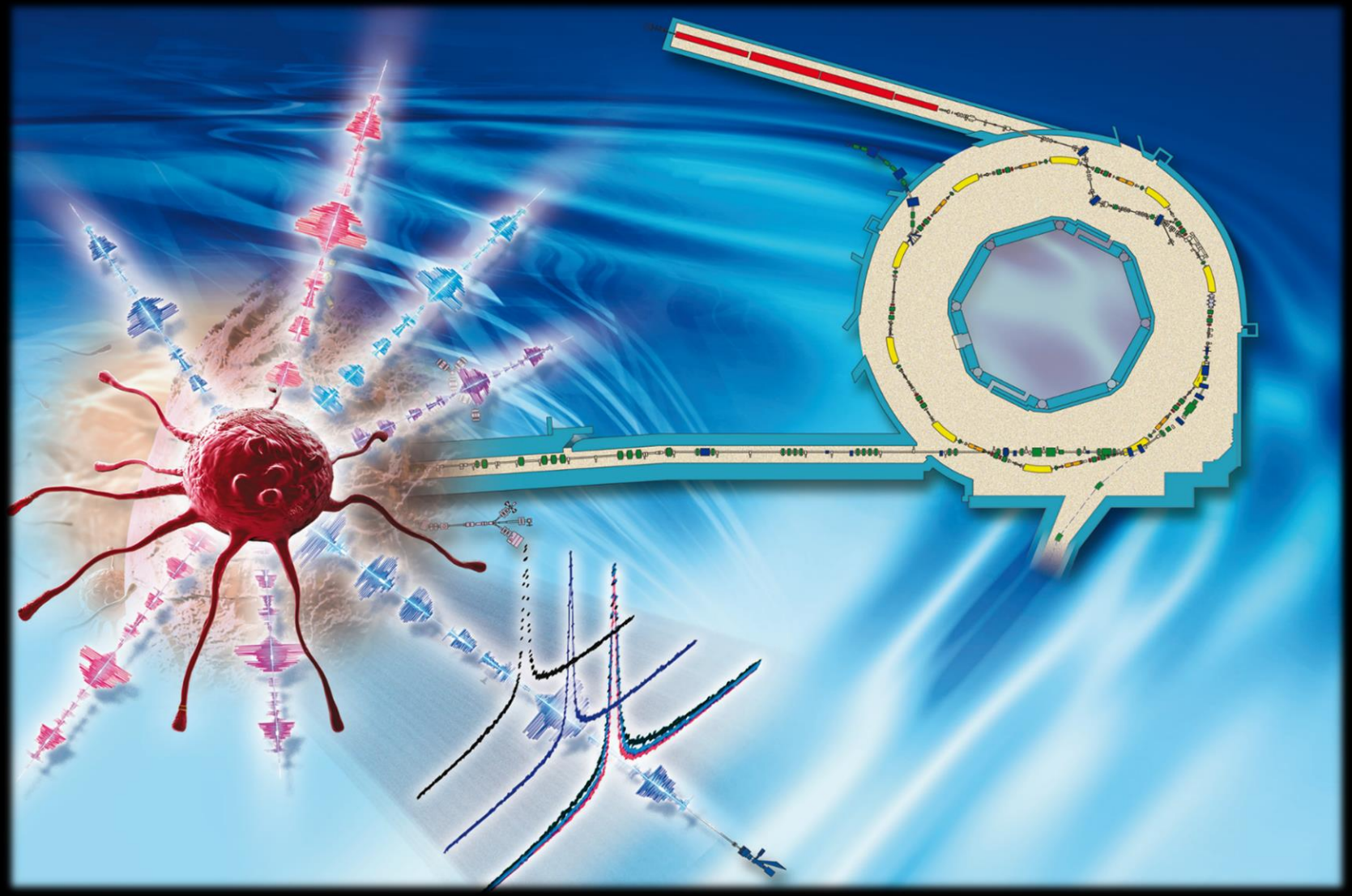
Shining the Beam on Water in Human Cells and Tissues

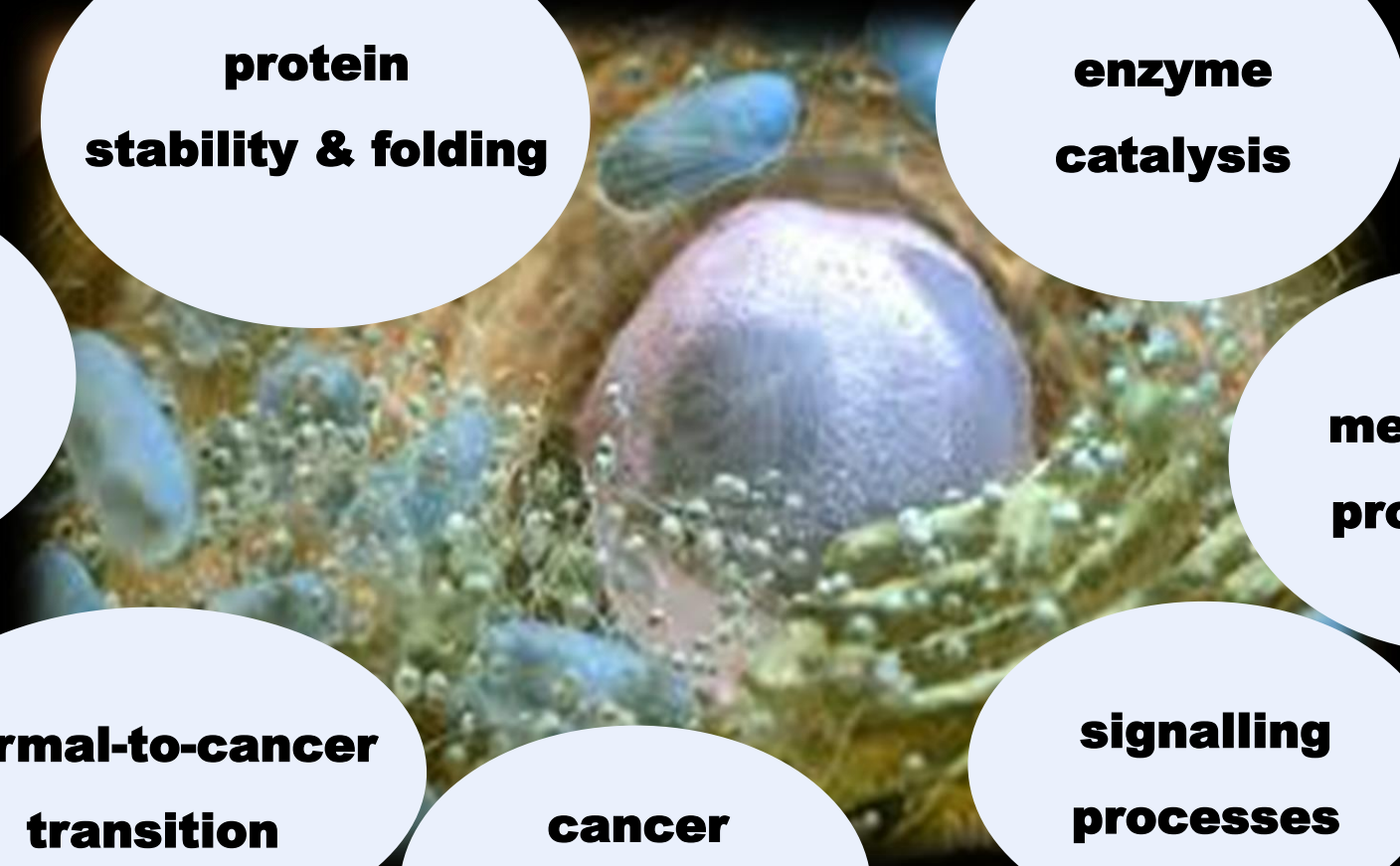


Maria Paula Marques

"Molecular Physical-Chemistry"
University of Coimbra PORTUGAL

INTRACELLULAR WATER

MAJOR CELLULAR CONSTITUENT



protein stability & folding

enzyme catalysis

DNA packaging

membrane properties

normal-to-cancer transition

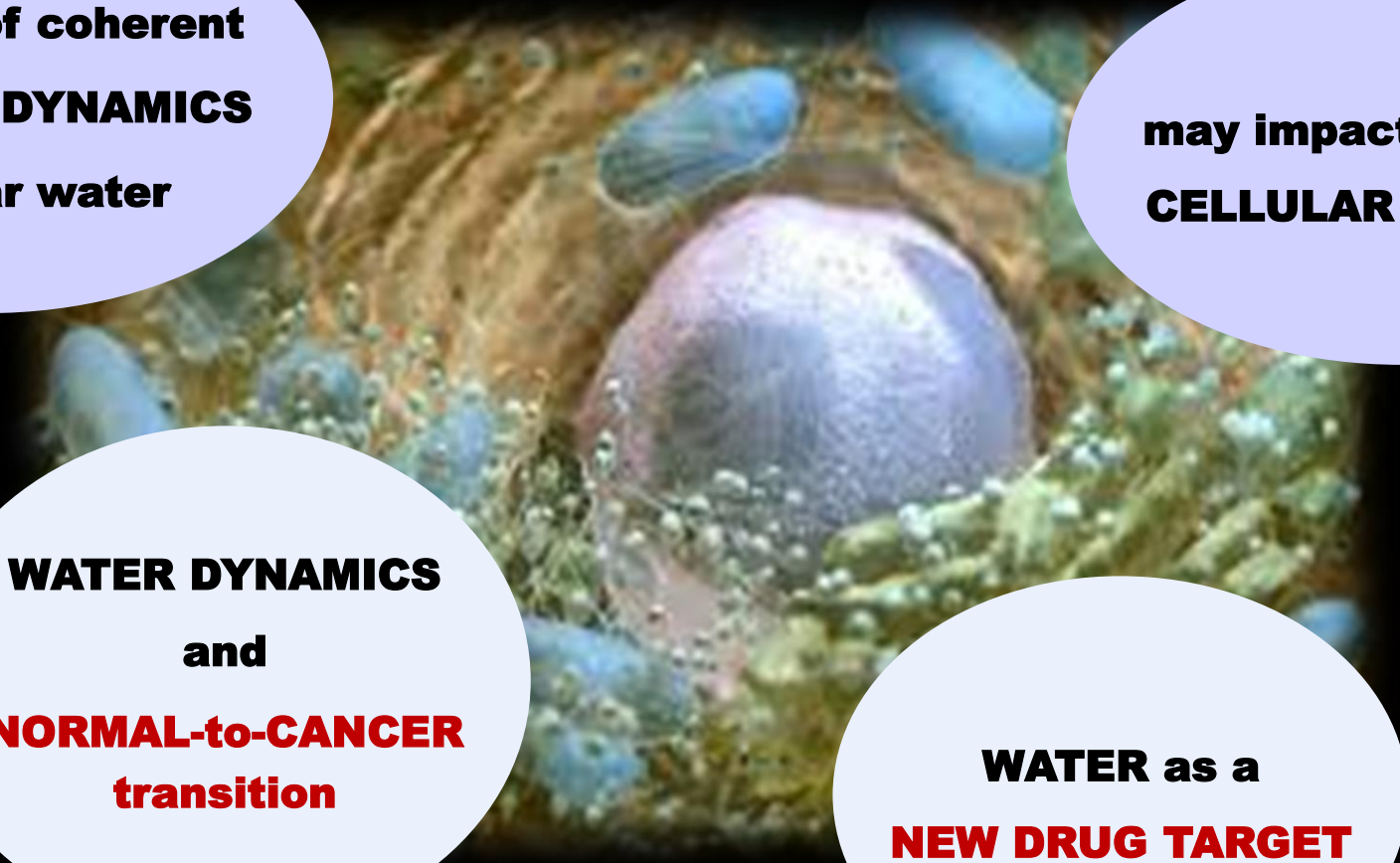
cancer invasiveness metastasis

signalling processes

Química-Física Molecular

INTRACELLULAR WATER DYNAMICS

disruption of coherent structure & DYNAMICS of cellular water



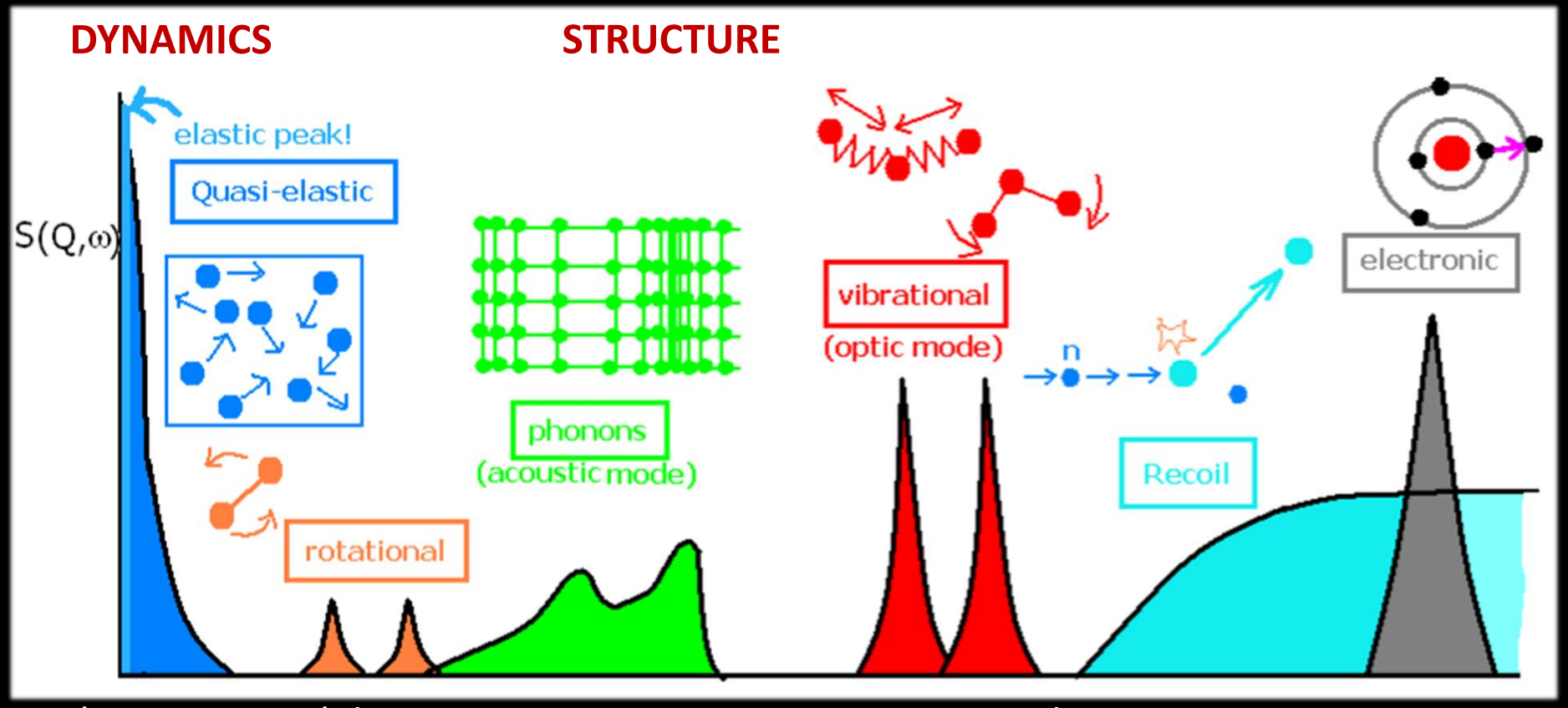
may impact on normal CELLULAR FUNCTION

WATER DYNAMICS and NORMAL-to-CANCER transition

WATER as a NEW DRUG TARGET

PROBED by VIBRATIONAL SPECTROSCOPY

quasi-elastic neutron scattering



QENS

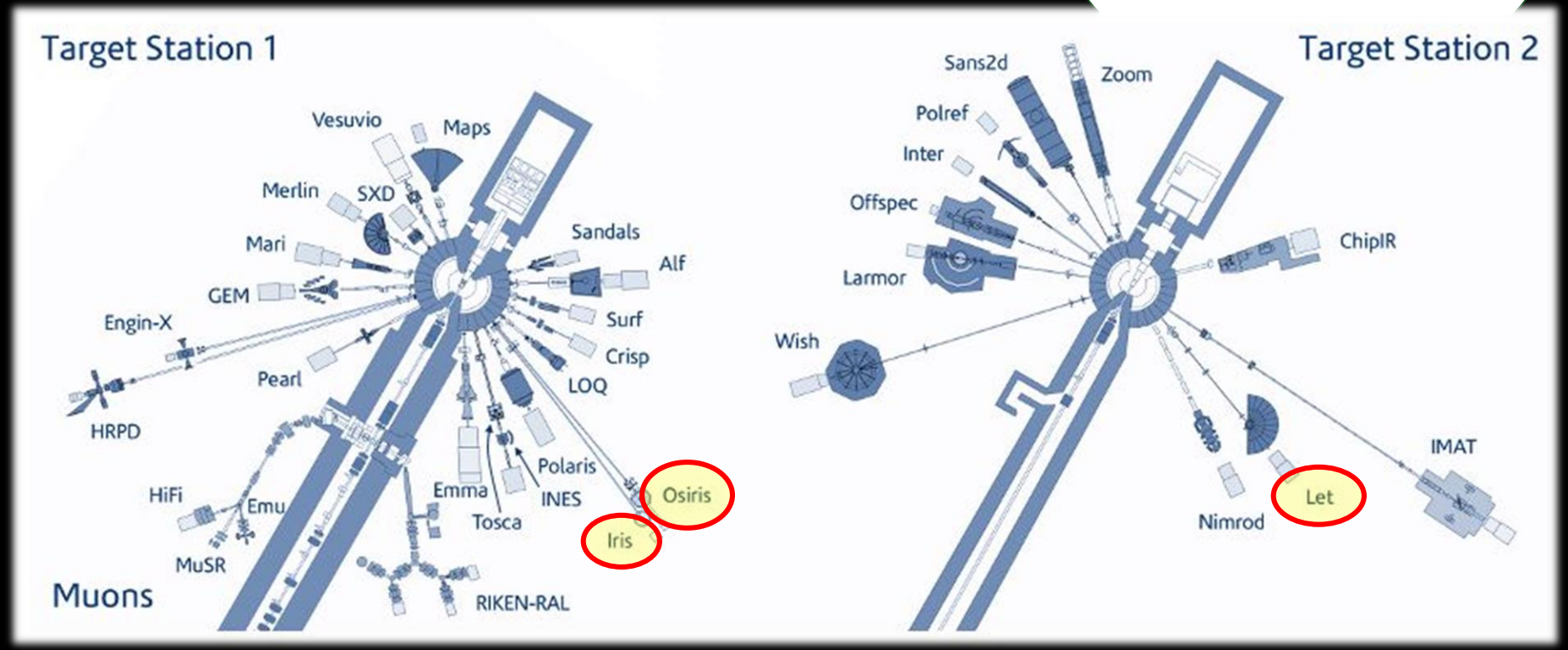
INS / FTIR / Raman

molecular vibrations

Química-Física Molecular


ISIS
Chilton, UK

ISIS



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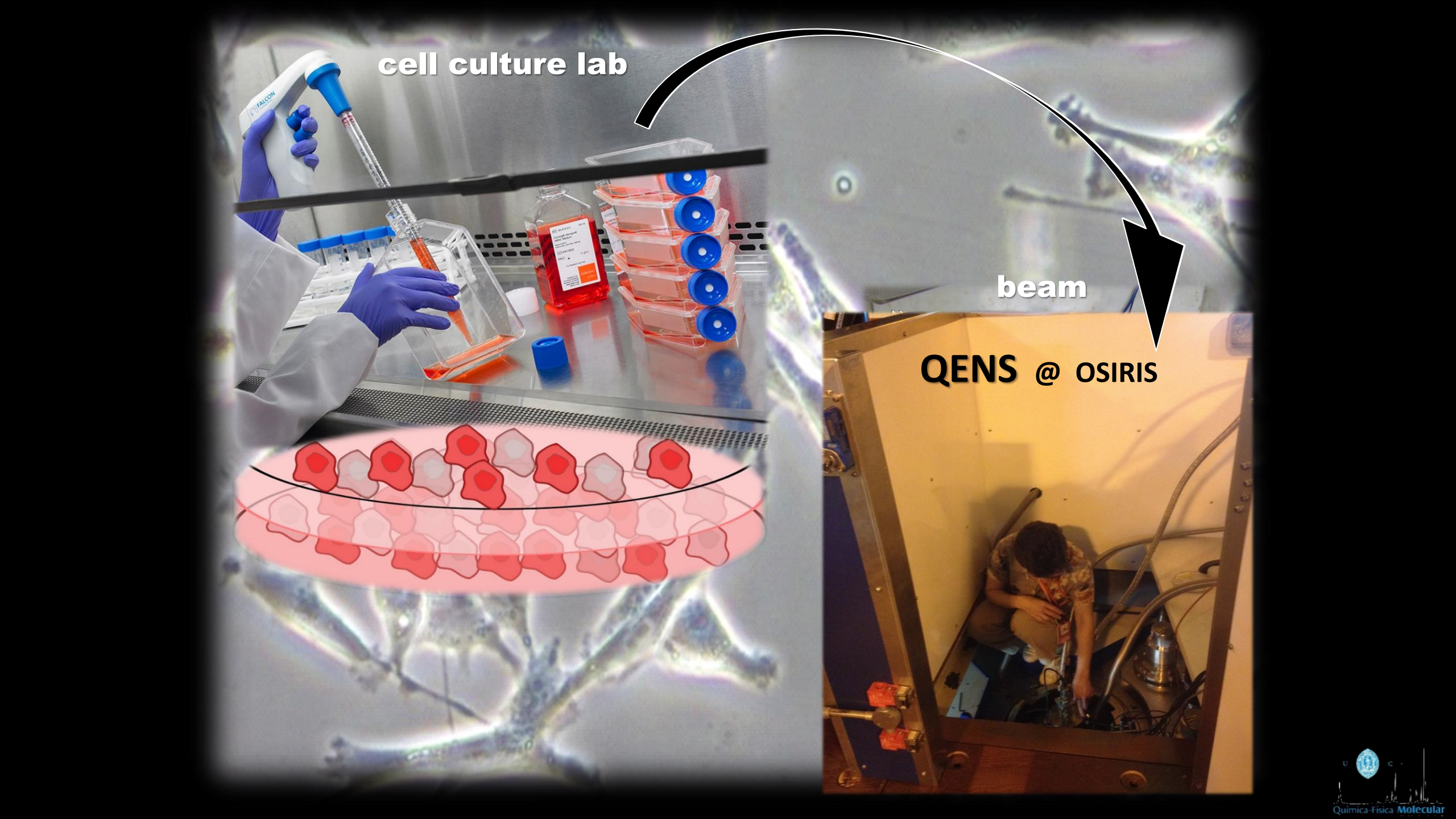
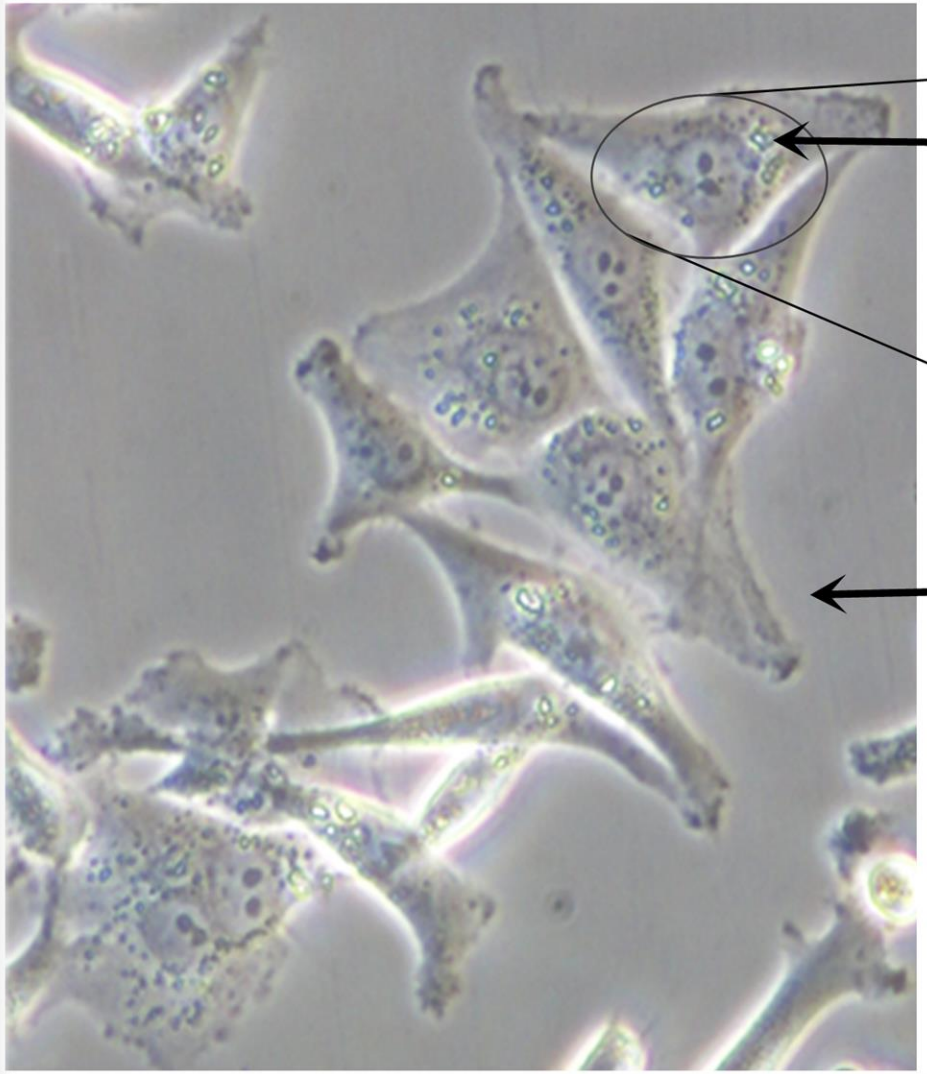
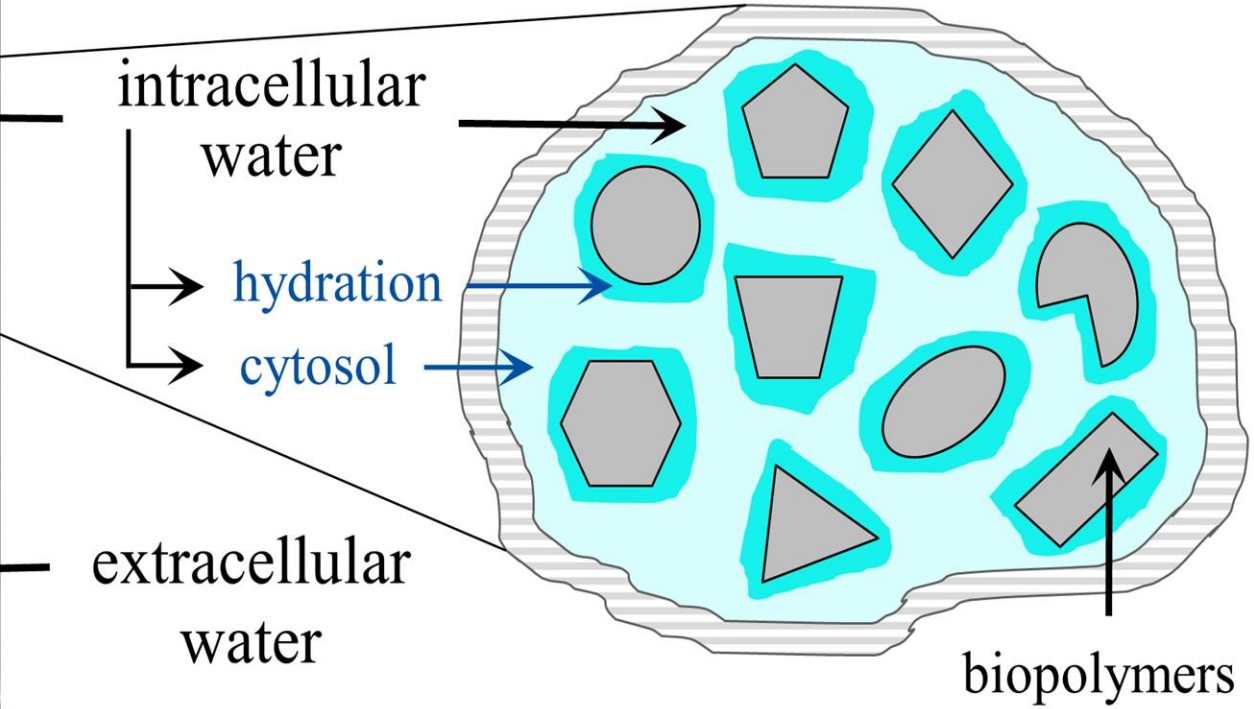
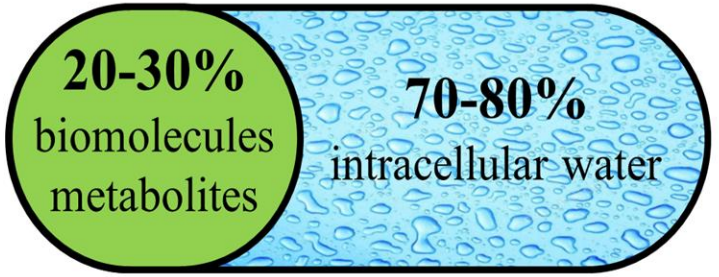

cell culture lab
beam
QENS @ OSIRIS

cells/tissues – different types of intracelular water



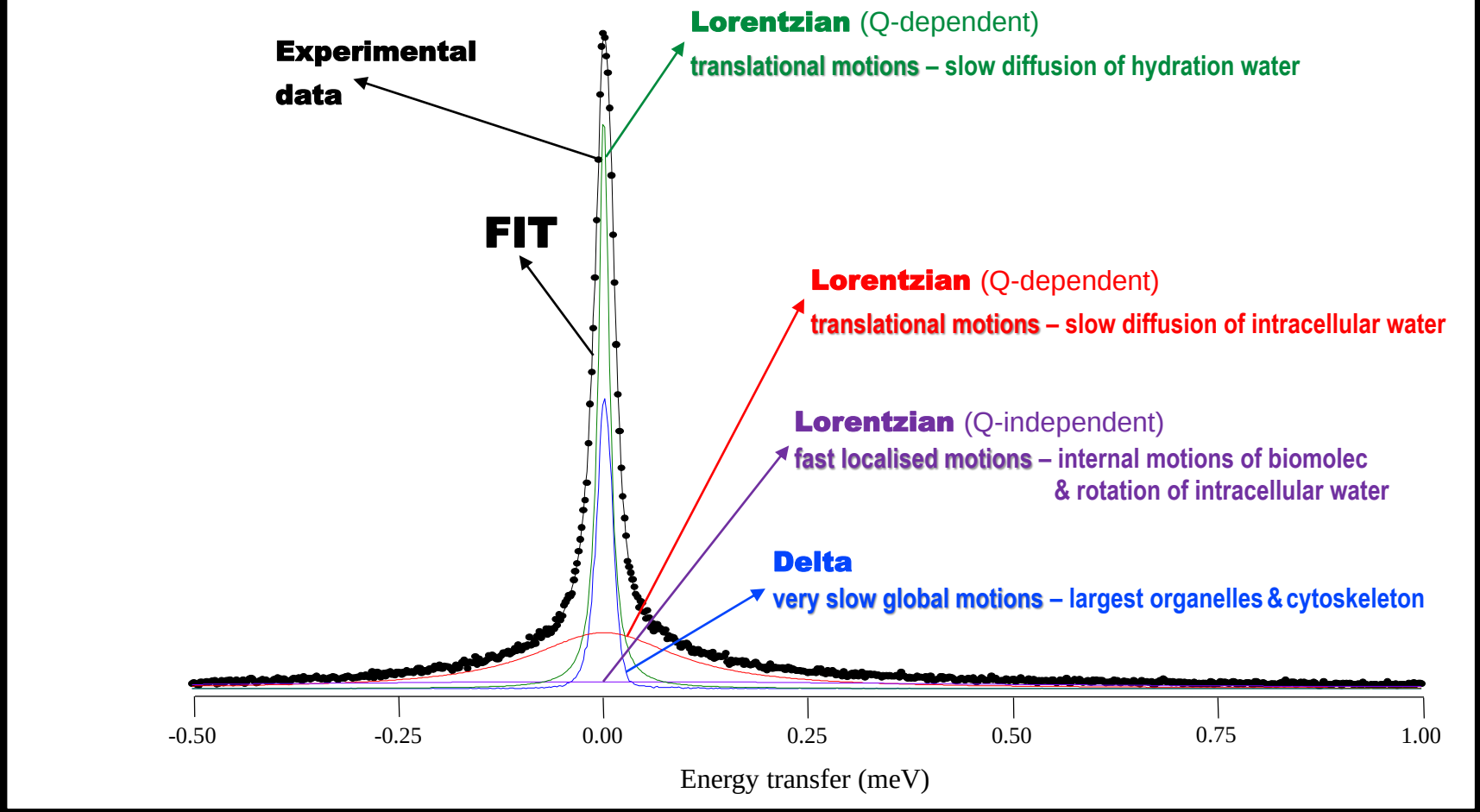




fitting QENS data
to represent the various dynamic componentes within the cell

1 Delta + 3 Lorentzians

cisplatin-treated cells (8 μM) – 298 K (human triple negative breast cancer)



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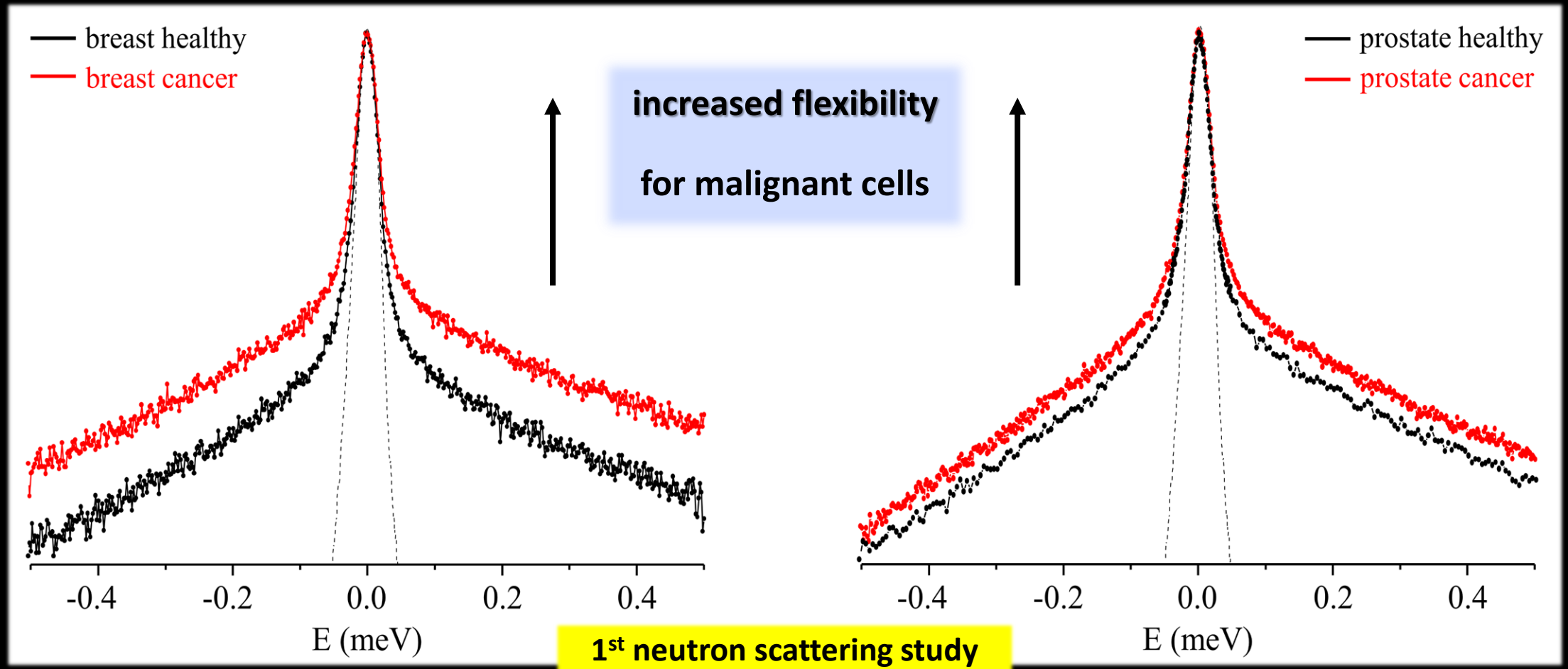
HUMAN CELLS – healthy *vs* cancer

prostate cancer / triple-negative breast cancer

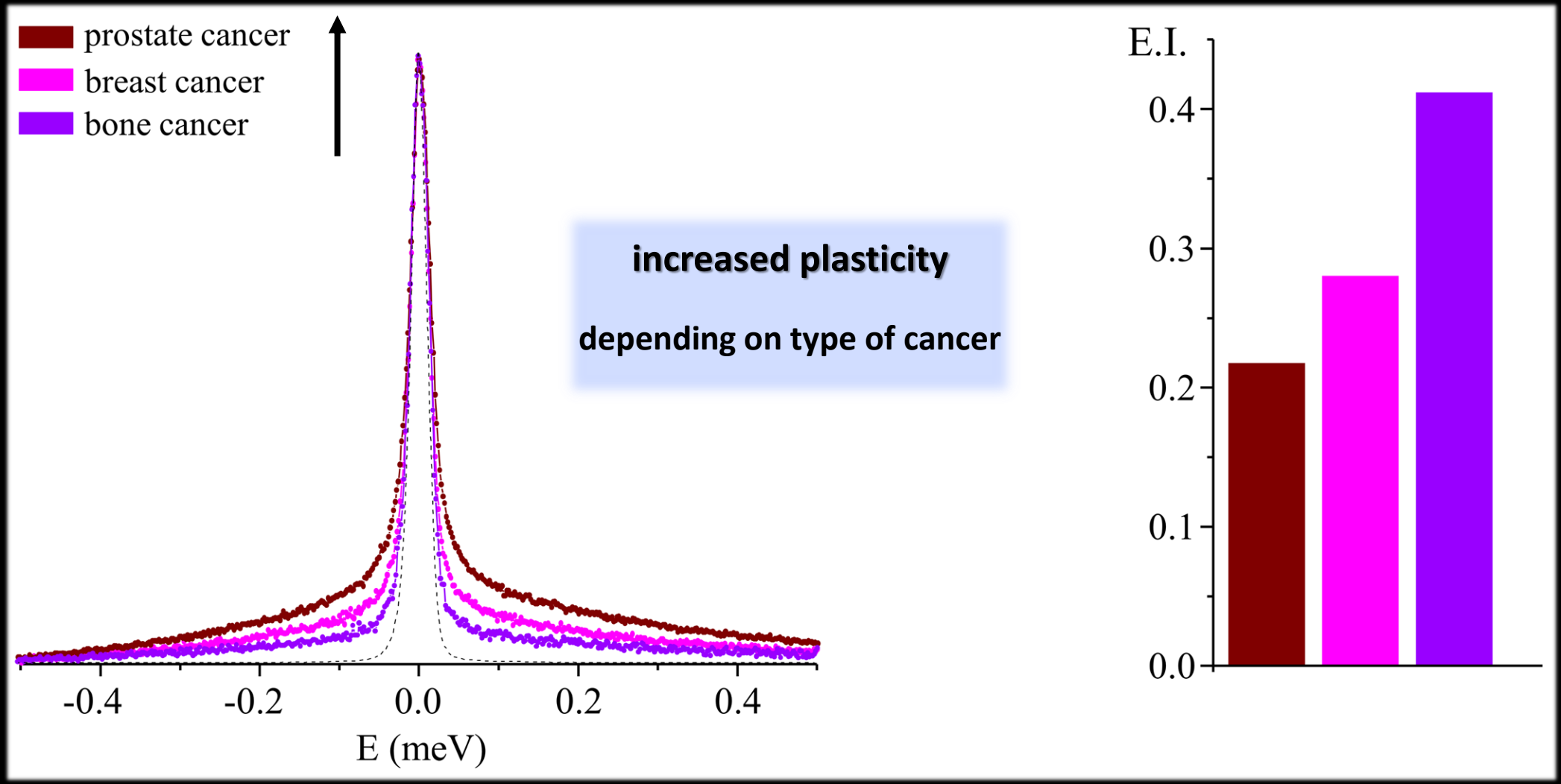


1st neutron scattering study on cancer *versus* healthy cells

Marques *et al. PCCP* 19 (2017) 2702; Marques *et al. Int.Rev.Phys.Chem.* 39 (2020) 67; Marques *et al. Struct.Dyn.* 7 (2020) 054701; Batista Carvalho *et al. Biophys.J.* 120 (2021) 3070

HUMAN CANCER CELLS – diferent types of cancer

prostate cancer / triple-negative breast cancer / osteosarcoma



HUMAN TISSUES – healthy *vs* cancer

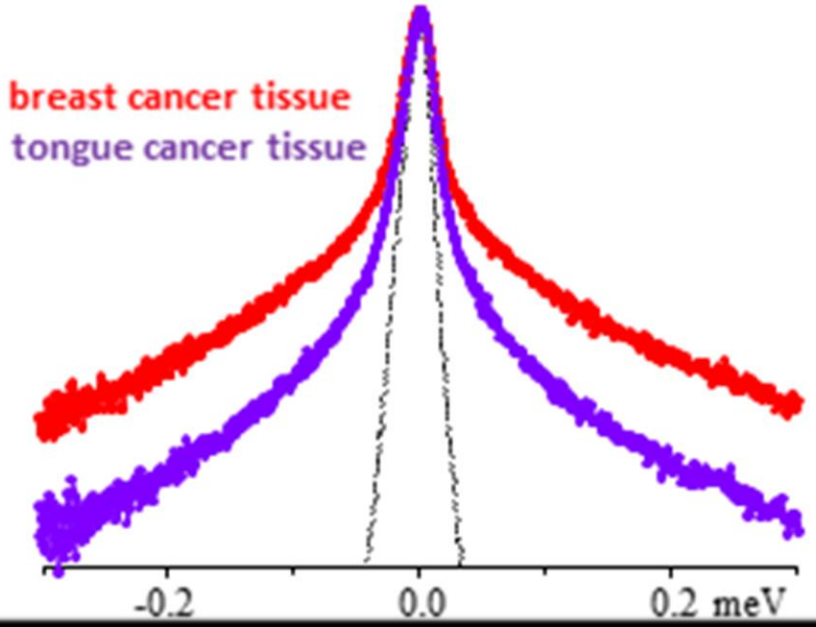
resection specimens from breast and tongue cancer patients

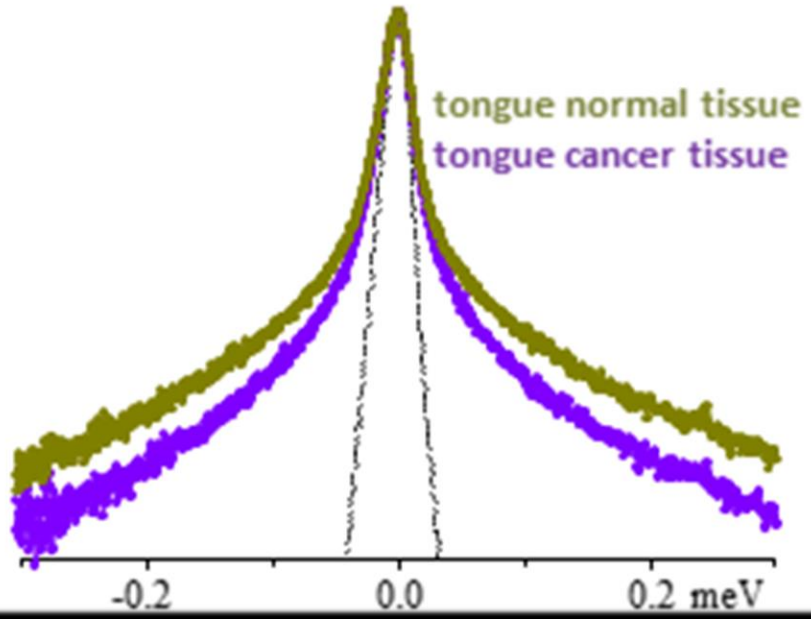
bulk tumour *vs* tumour-free surrounding area

distinct dynamical behaviour

depending on

healthy *vs* malignant
type of cancer





Marques *et al. PCCP* 24 (2022) 15406

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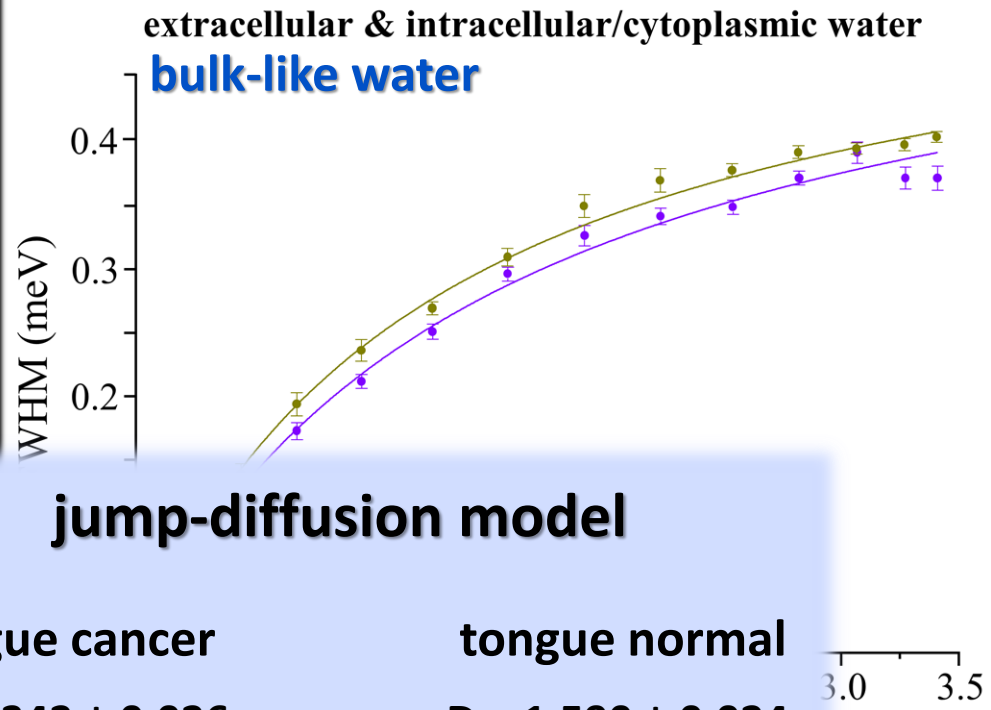
HUMAN TISSUES – healthy *vs* cancer

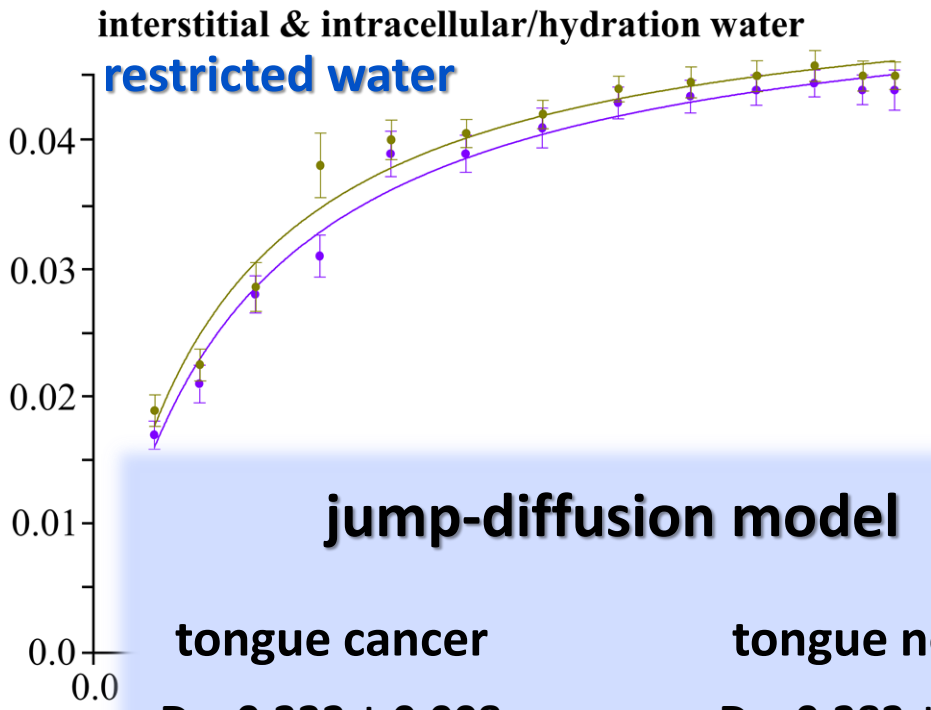
resection specimens from patients – breast and tongue cancer

bulk tumour *vs* tumour-free surrounding area

tongue normal tissue

tongue cancer tissue





jump-diffusion model

tongue cancer	tongue normal
D = 1.342 ± 0.026	D = 1.590 ± 0.024
τ = 1.158 ± 0.042	τ = 1.165 ± 0.023

jump-diffusion model

tongue cancer	tongue normal
D = 0.332 ± 0.008	D = 0.383 ± 0.011
τ = 12.410 ± 0.239	τ = 12.389 ± 0.248

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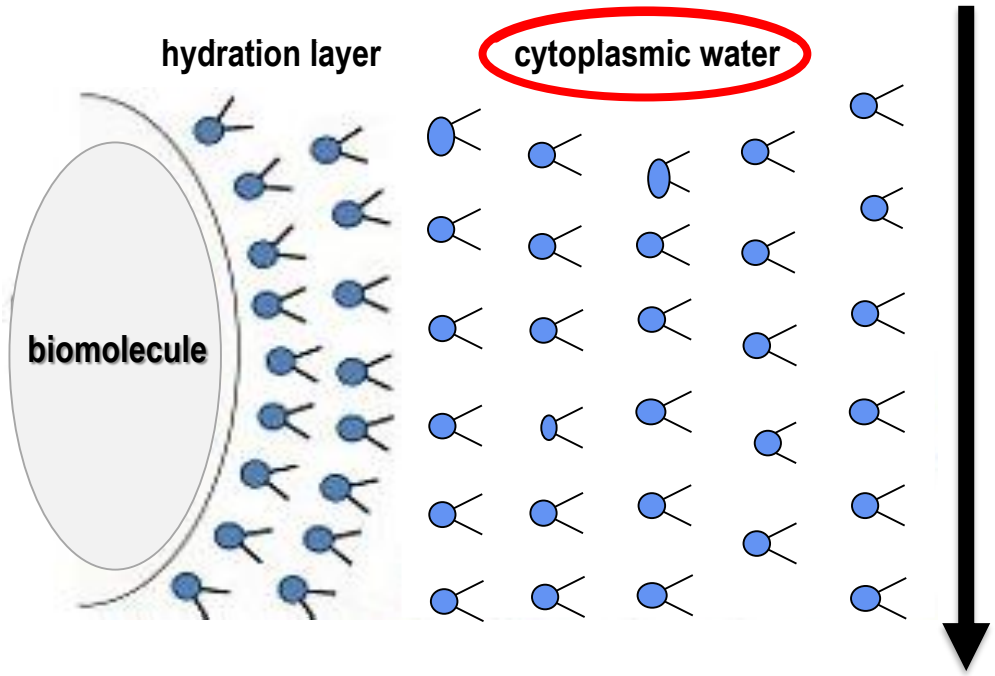
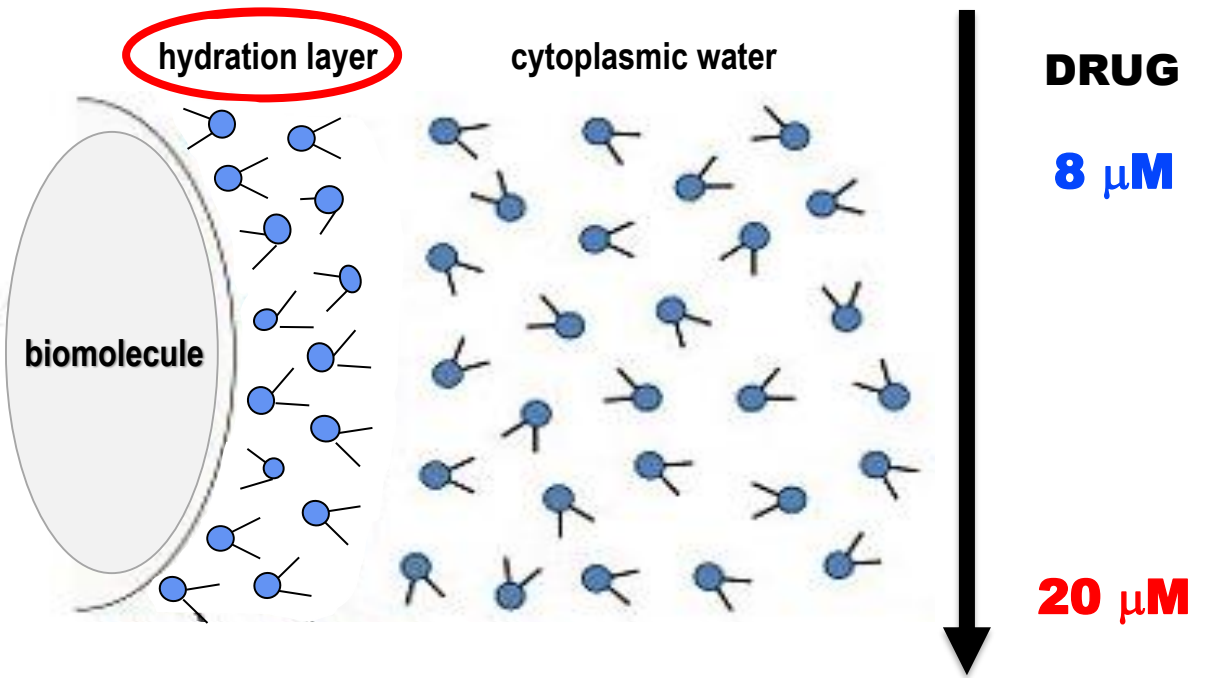
HUMAN CELLS – Drug effect

cisplatin-8 μM – impact on intracelular water/breast cancer



drug-prompted increase in organisation
restricted mobility



drug-prompted disruption of the hydration layers
higher mobility

Marques *et al. PCCP* 19 (2017) 2702; Batista Carvalho *et al. PCCP* 21 (2019) 4162; Marques *et al. Molecules* 25 (2020) 246

INTRACELLULAR WATER DYNAMICS

understand NTC transition

at the molecular level

improved chemotherapeutic approaches

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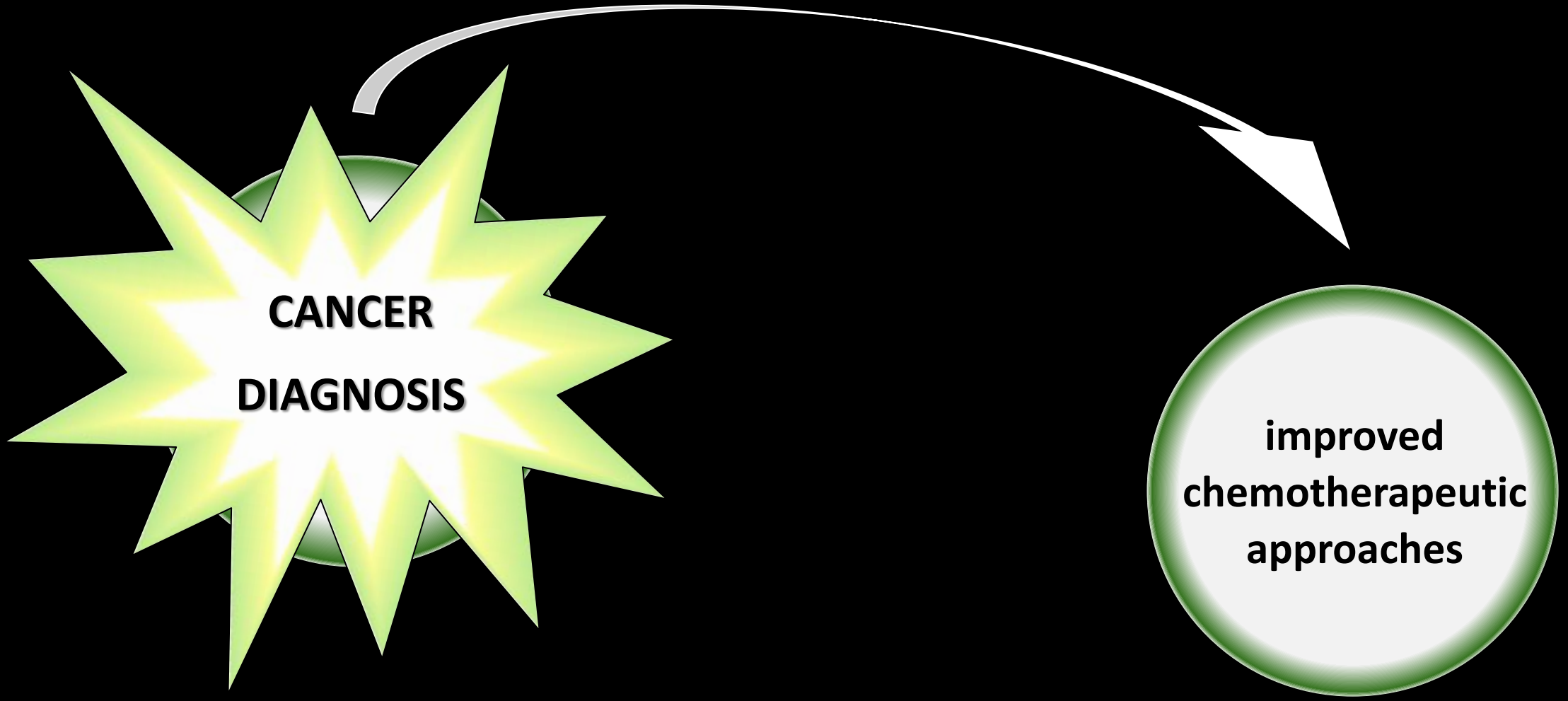
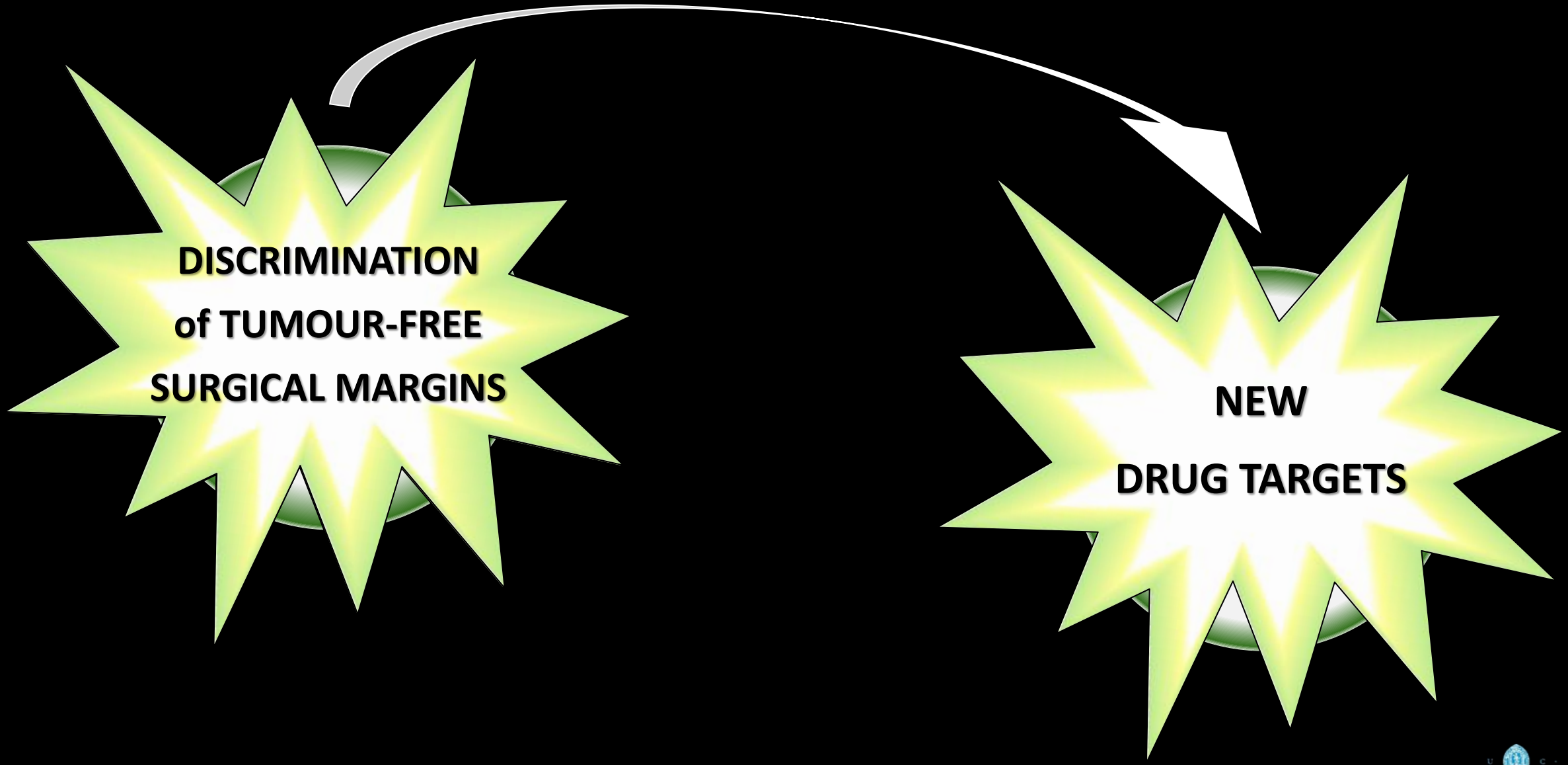
INTRACELLULAR WATER DYNAMICS



INTRACELLULAR WATER DYNAMICS



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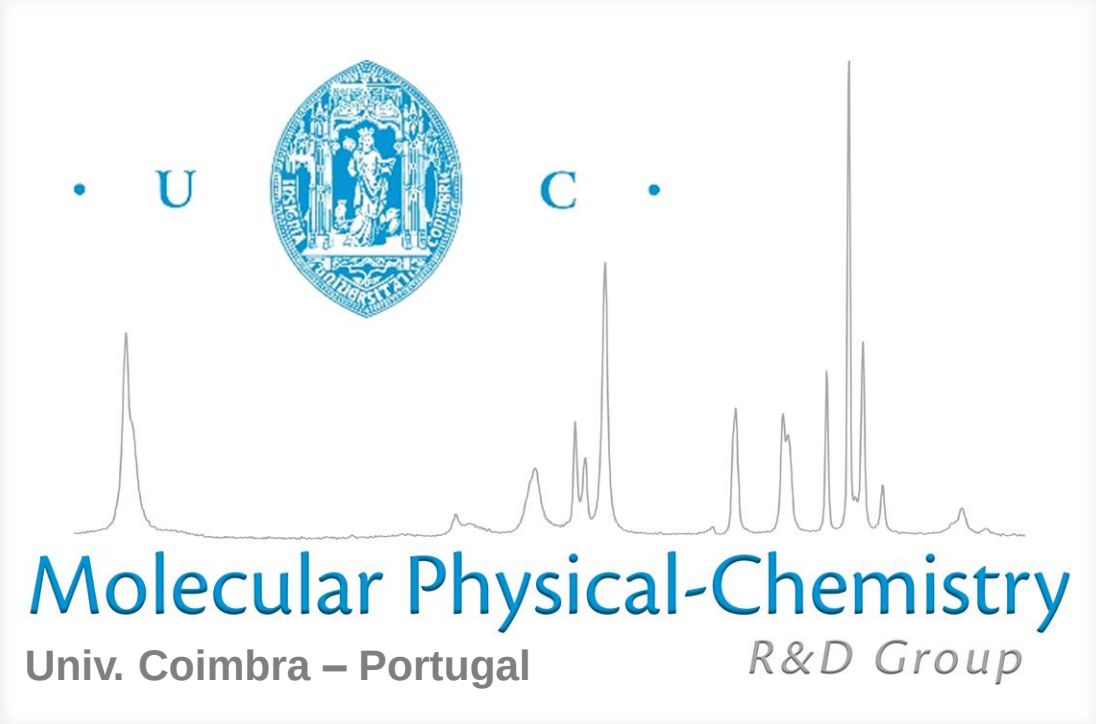

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