LENS LEAGUE OF ADVANCED EUROPEAN NEUTRON SOURCES

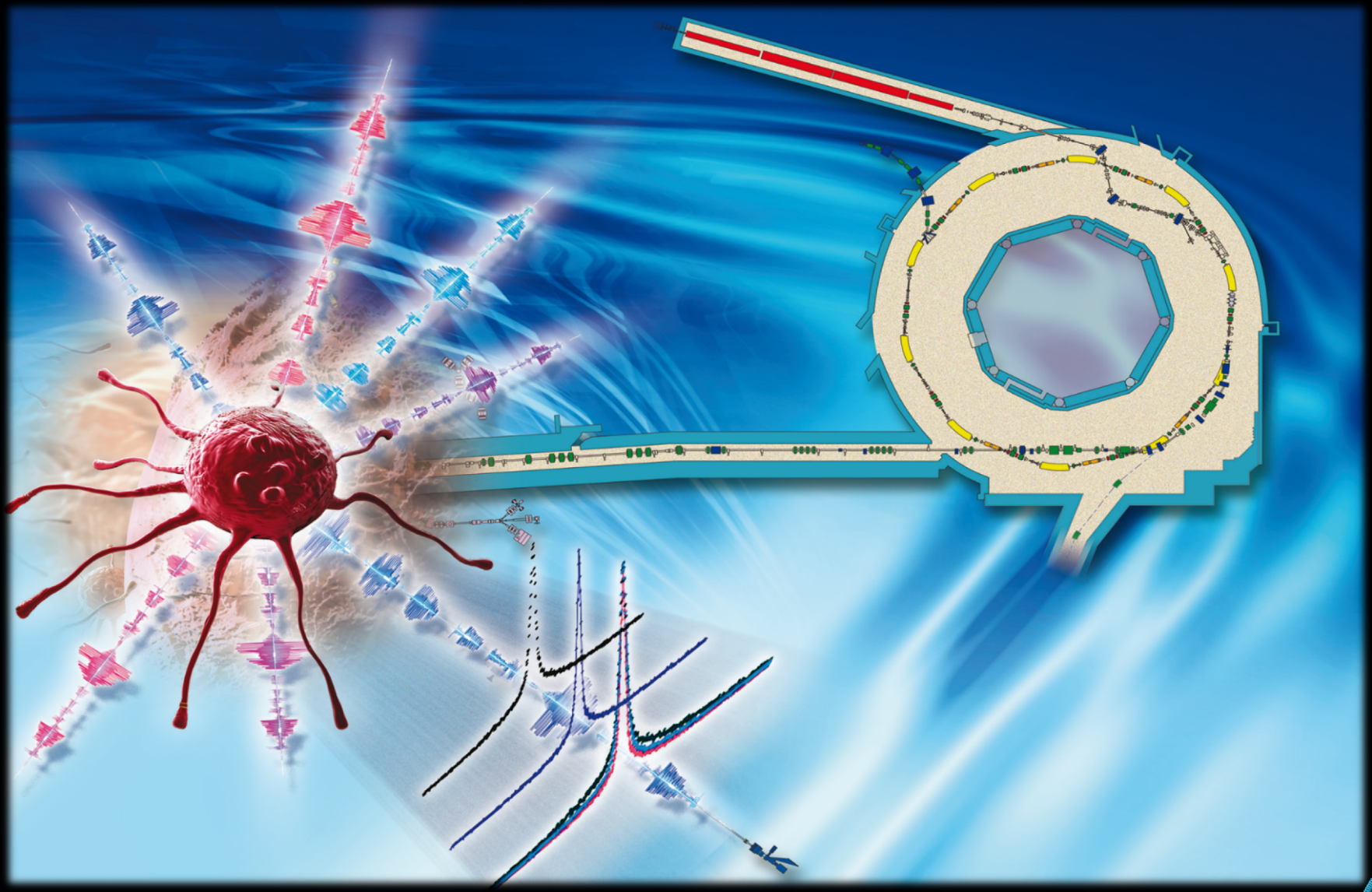
Neutrons and Human Health: from Anticancer Drugs to Bone Analysis

Maria Paula M. Marques: Molecular Physical-Chemistry R&D Group, Universidade de Coimbra

brightness²

BrightnESS² is funded by the European Union Framework Programme for Research and Innovation Horizon 2020, under grant agreement 823867

Neutrons and Human Health from Anticancer Drugs to Bone Analysis



Maria Paula Marques

"Molecular Physical-Chemistry"
University of Coimbra PORTUGAL

the Portuguese

neutron users community

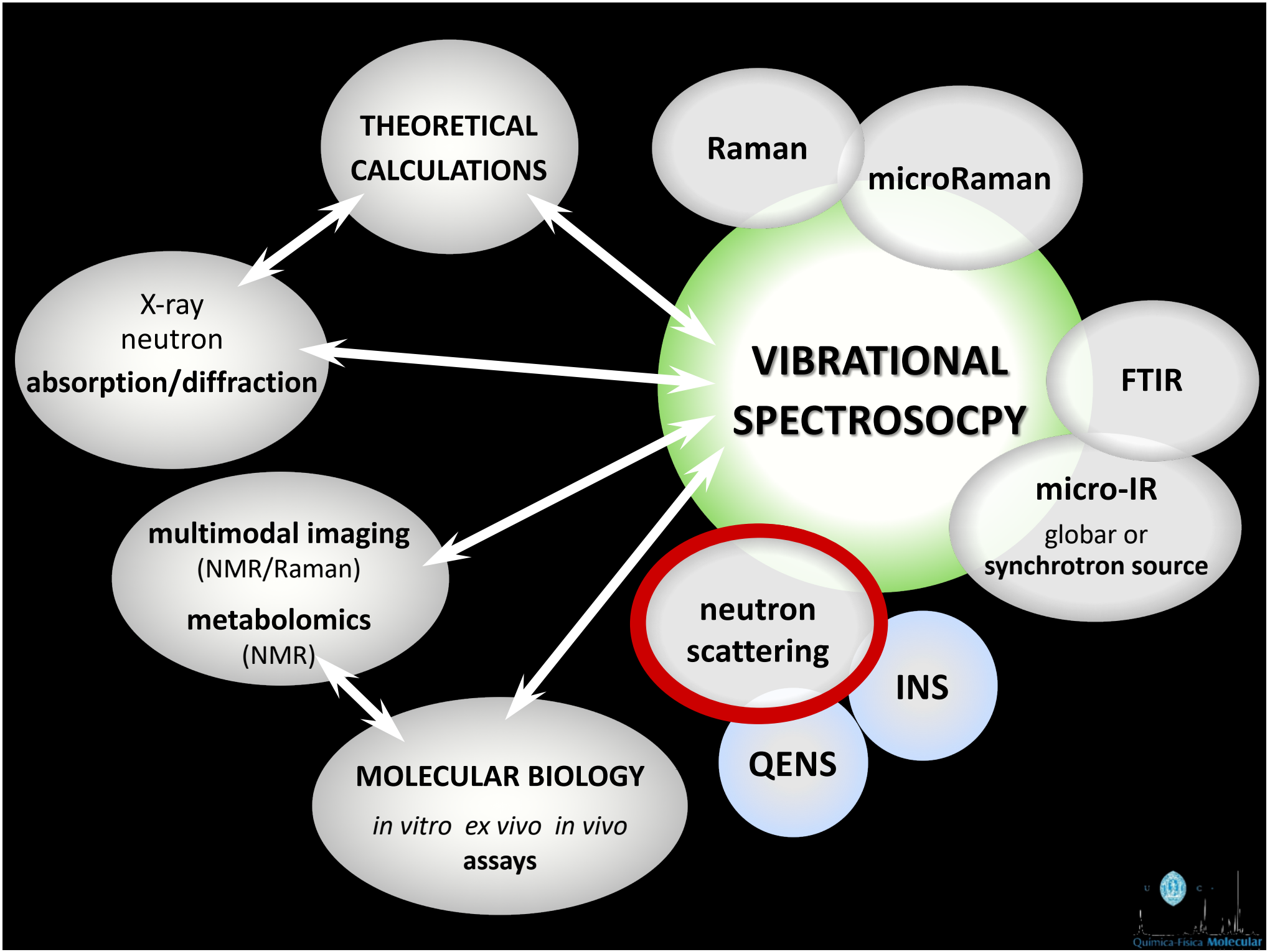
NeMPo – **https://fisica-materia-condensada.spf.pt/NeMPo**

· U C ·

Molecular Physical-Chemistry

R&D Group

Química-Física Molecular

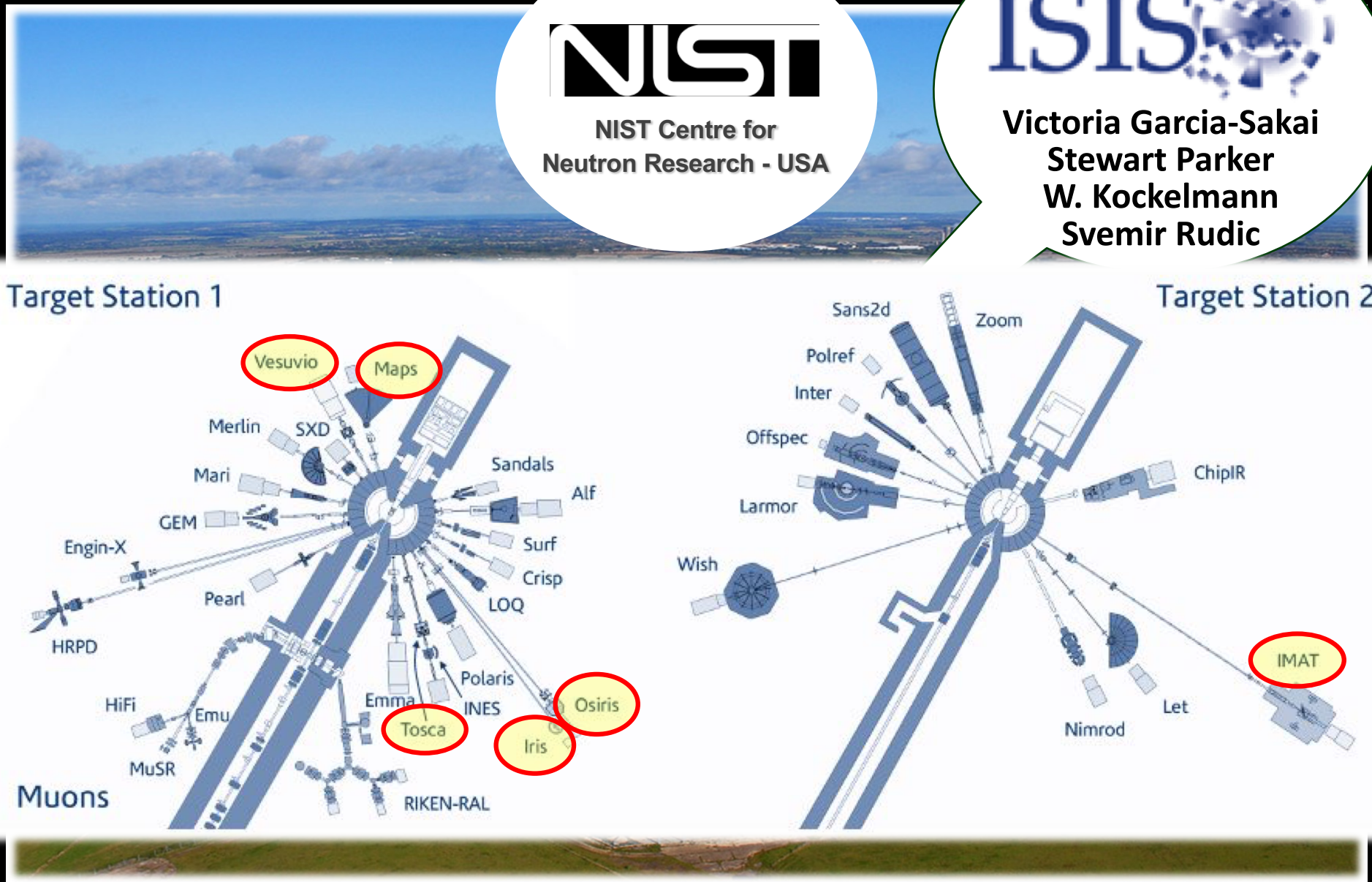

THEORETICAL CALCULATIONS
Raman
microRaman
X-ray
neutron
absorption/diffraction
VIBRATIONAL SPECTROSOCPY
FTIR
micro-IR
globar or
synchrotron source
multimodal imaging
(NMR/Raman)
metabolomics
(NMR)
neutron scattering
INS
QENS
MOLECULAR BIOLOGY
in vitro ex vivo in vivo
assays
Química-Física Molecular

NEUTRON SCATTERING - Inelastic and Quasi-elastic Spectroscopy

NIST Centre for Neutron Research - USA

ISIS

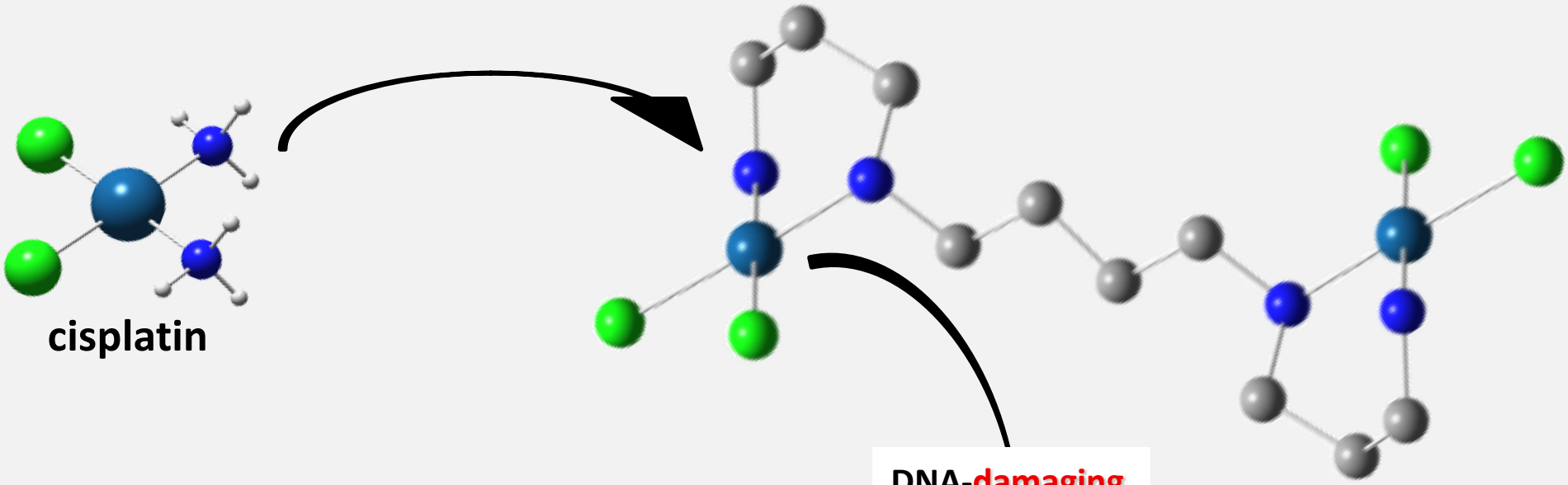
Victoria Garcia-Sakai
Stewart Parker
W. Kockelmann
Svemir Rudic



new
anticancer agents

identification
burned human
skeletal remains

metal-based ANTICANCER AGENTS



cisplatin

DNA-damaging
covalent bonding

main pharmacological
TARGET

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MULTITARGET APPROACH

improve

effectiveness

&

minimise

toxicity/resistance

searching for new DRUG TARGETS

may a drug effect

the highly crowded intracelular medium?

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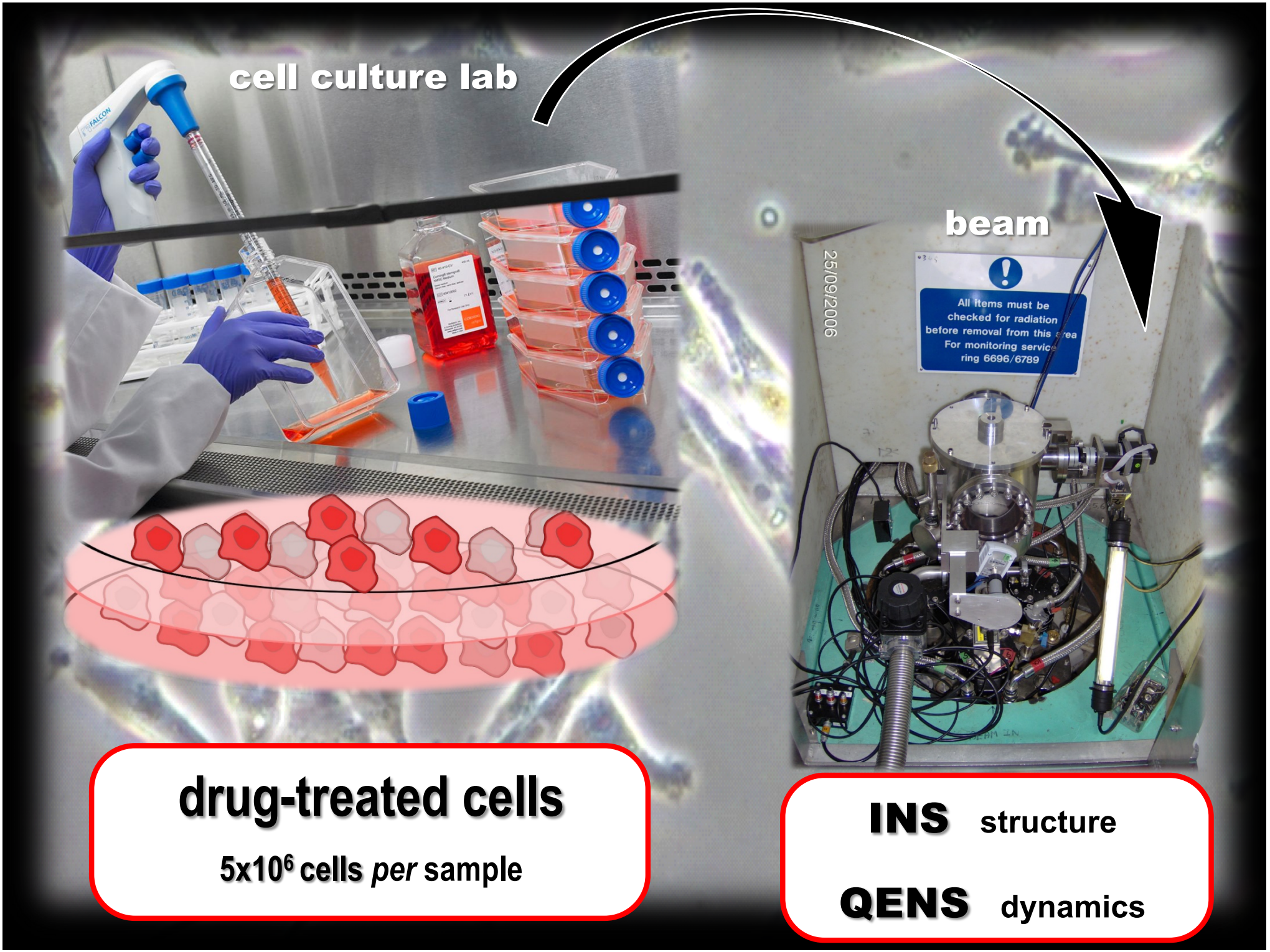
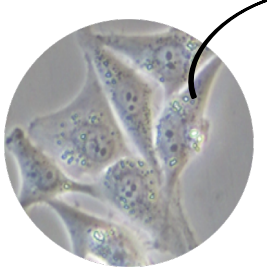

cell culture lab
beam
25/09/2006
All items must be checked for radiation before removal from this area
For monitoring service ring 6696/6789
drug-treated cells
5x10⁶ cells per sample
INS structure
QENS dynamics

Quasi-elastic NEUTRON SCATTERING

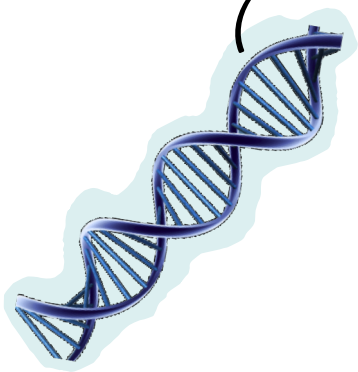
effect on INTRACELLULAR WATER – cytoplasm
biomolecule´s hydration layers

INTRACELLULAR WATER
cytoplasm
drug-prompted
RESTRICTED MOBILITY



control
drug

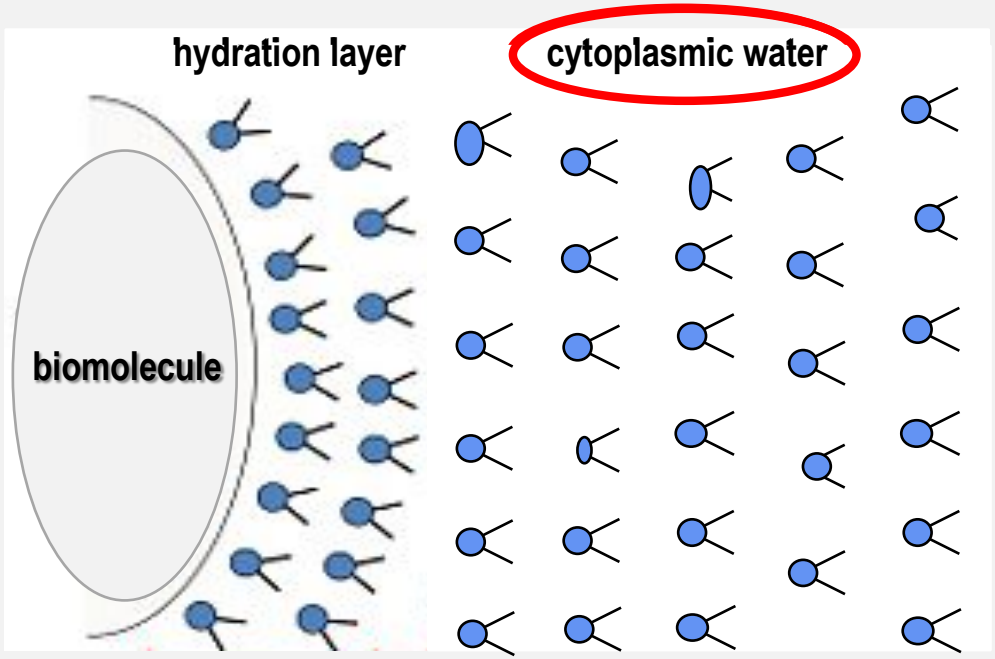
DNA´s HYDRATION WATER
drug-prompted
INCREASED MOBILITY



Marques *et al. PCCP* 19 (2017) 2702. Marques *et al.*, *J.Phys.Chem.B* 123 (2019) 6968. Marques *et al.*, *Molecules* 25 (2020) 246.
Batista de Carvalho *et al. PCCP* 21 (2019) 4162. Marques *et al.*, *Int.Rev.Phys.Chem.* 39 (2020) 67.

proposed interpretation of the data

drug effect on cytoplasmic water



DRUG

8 μM

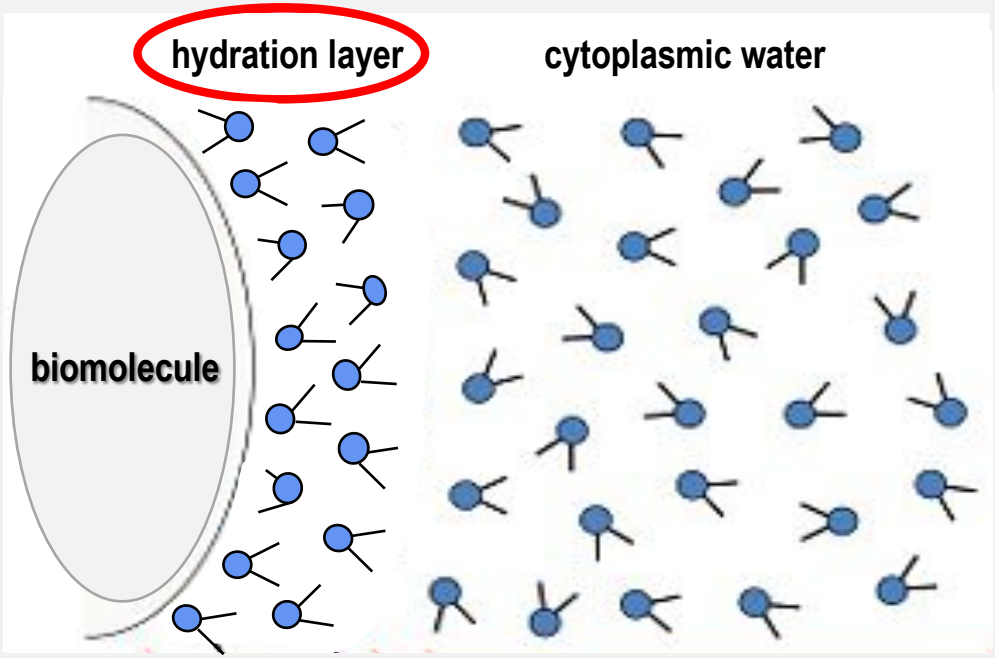
drug-prompted
concentration-dependent
restricted mobility

20 μM

drug-triggered reorganisation of H-bonding network

proposed interpretation of the data

drug effect on hydration water



DRUG

8 μM

drug-prompted disruption
of the hydration layers

20 μM

associated to

drug-triggered conformational changes in biomolecules

Química-Física Molecular

distinct impact

for different drugs

Pt *vs* Pd

dynamics probed

at **ps & ns**

timescales

different

intracellular water dynamics

for **malignant *vs* healthy cells**

PCCP

PAPER

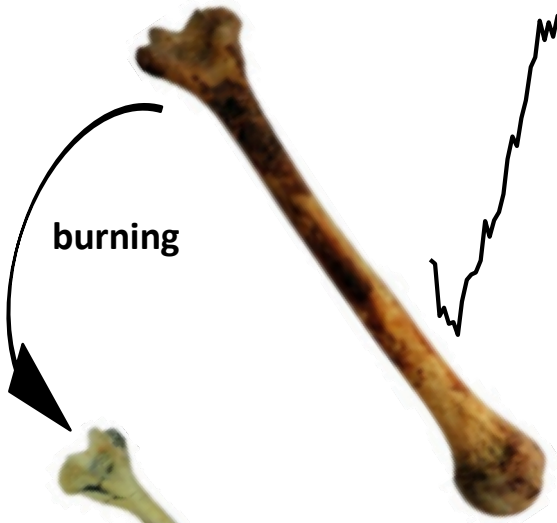
View Article Online
View Journal

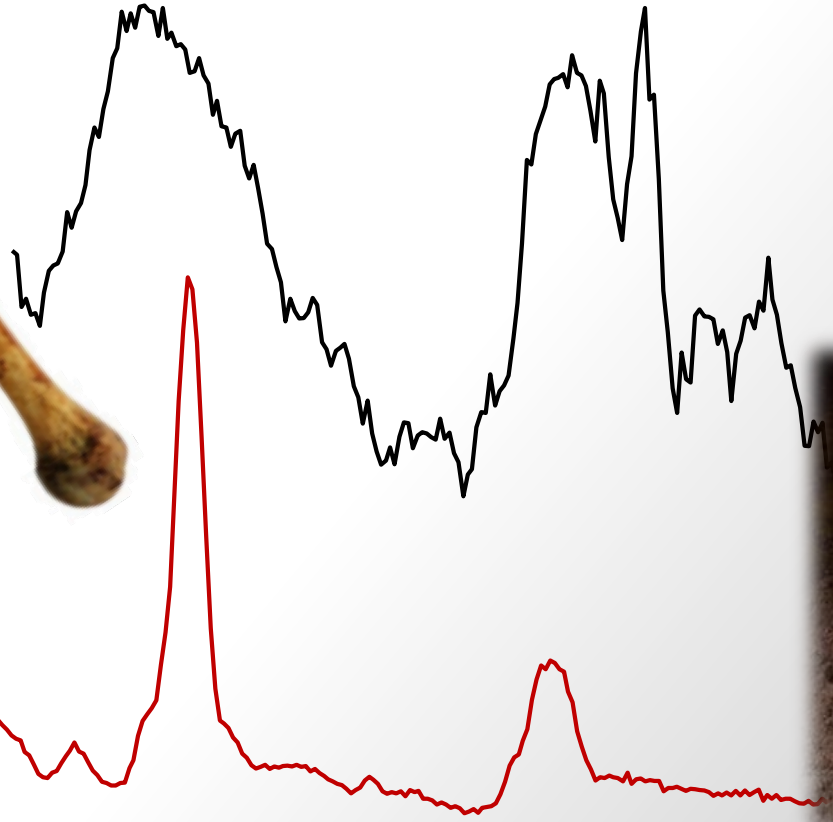
Cite this: DOI: 10.1039/c6cp05198g

Intracellular water – an overlooked drug target? Cisplatin impact in cancer cells probed by neutrons†

M. P. M. Marques,‡*[ab] A. L. M. Batista de Carvalho,‡*[a] V. Garcia Sakai,[c] L. Hatter[d] and L. A. E. Batista de Carvalho[a]

characterisation of HUMAN BURNED BONES





AIM – identification of victim´s from fires/explosions

archaeological studies

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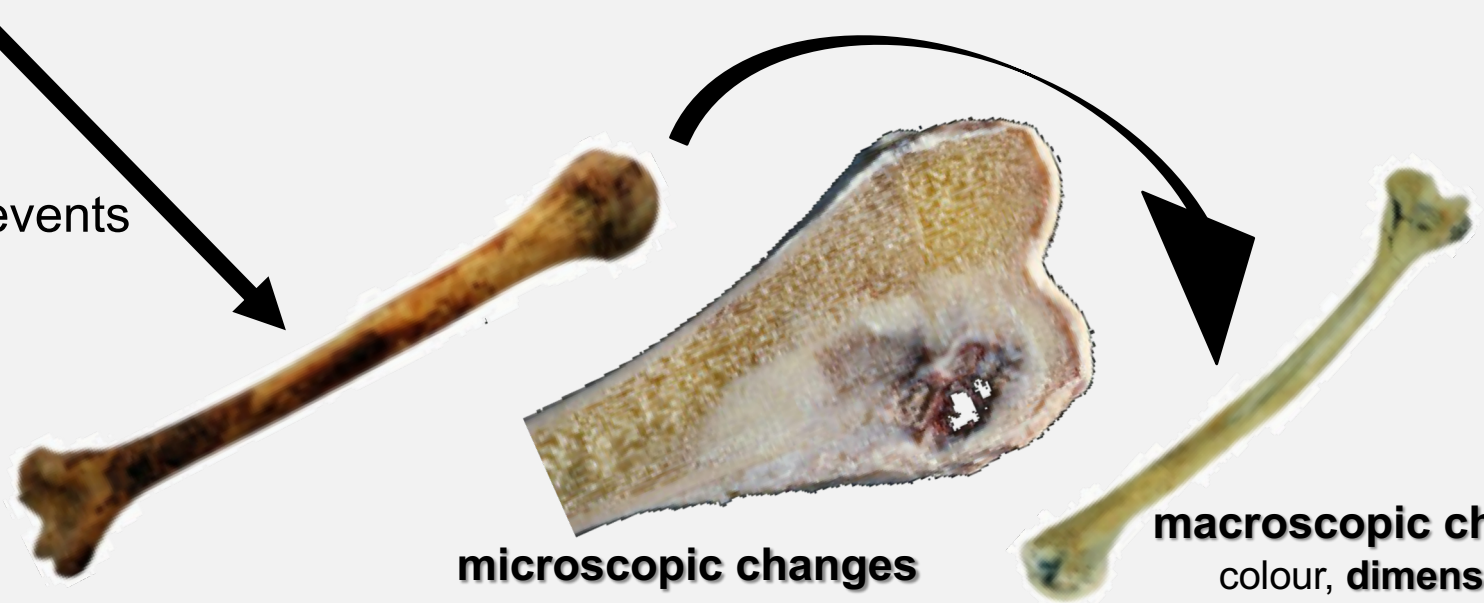
Burned Skeletal Remains

heat
burning events



microscopic changes
crystallinity

macroscopic changes
colour, **dimensions**

osteometrics for unburned bones
is inapplicable

NO CHARACTERISATION
is possible

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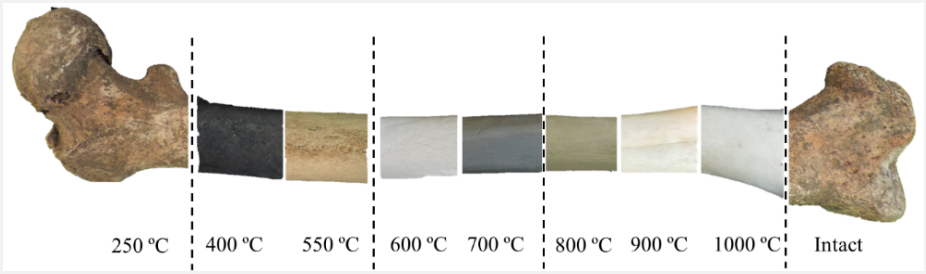
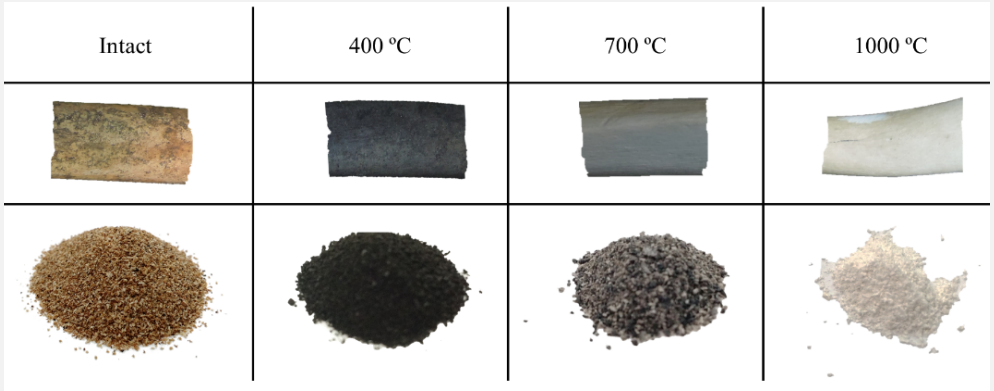
modern human bones
burned at controlled lab conditions



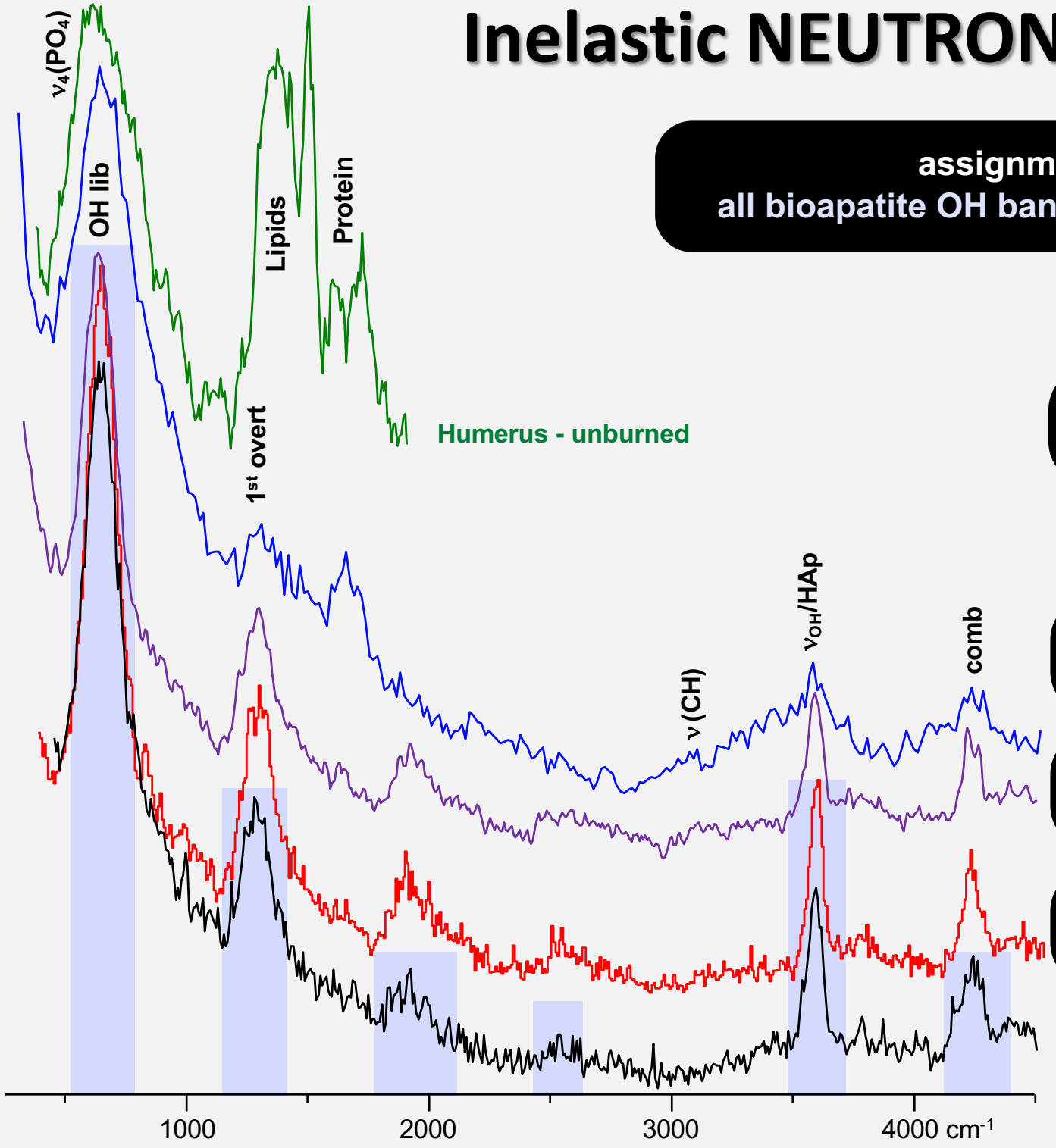
forensic & archaeological skeletal remains

REFERENCE COLLECTION → **REAL CASES**



RSC Adv. 6 (2016) 68638. *Am.J.Phys.Anthropol.* 166 (2018) 296. *RSC Adv.* 9 (2019) 36640.
RSC Adv. 8 (2018) 27260. *Anal.Chem.* 90 (2018) 11556. *Sci.Rep.* 8 (2018) 15935.

Inelastic NEUTRON SCATTERING



assignment of
all bioapatite OH bands in human bone

T

presence of protein and lipids

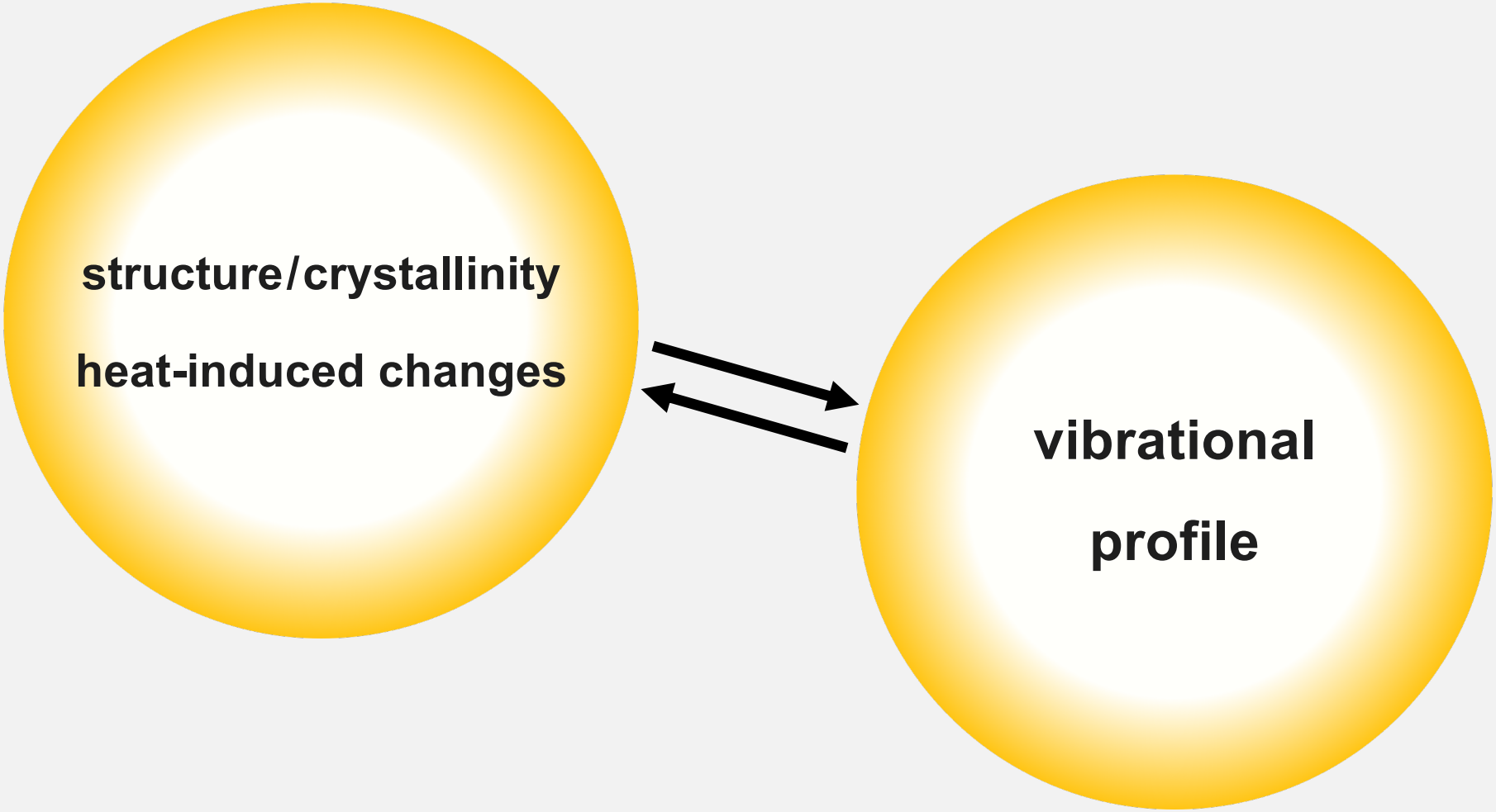
still presence of protein hardly any lipids

almost no protein nor lipids

no traces of organic constituents

HAp

Química-Física Molecular



identify reliable spectral biomarkers for routine use

quantitative relationship *unburn the bone*

Archaeological samples – human skeletal remains

A – Cencelle (Medieval)

C – Palestrina (Roman)

B – Scoglietto (Bronze Age)

D – Guidonia (Roman)

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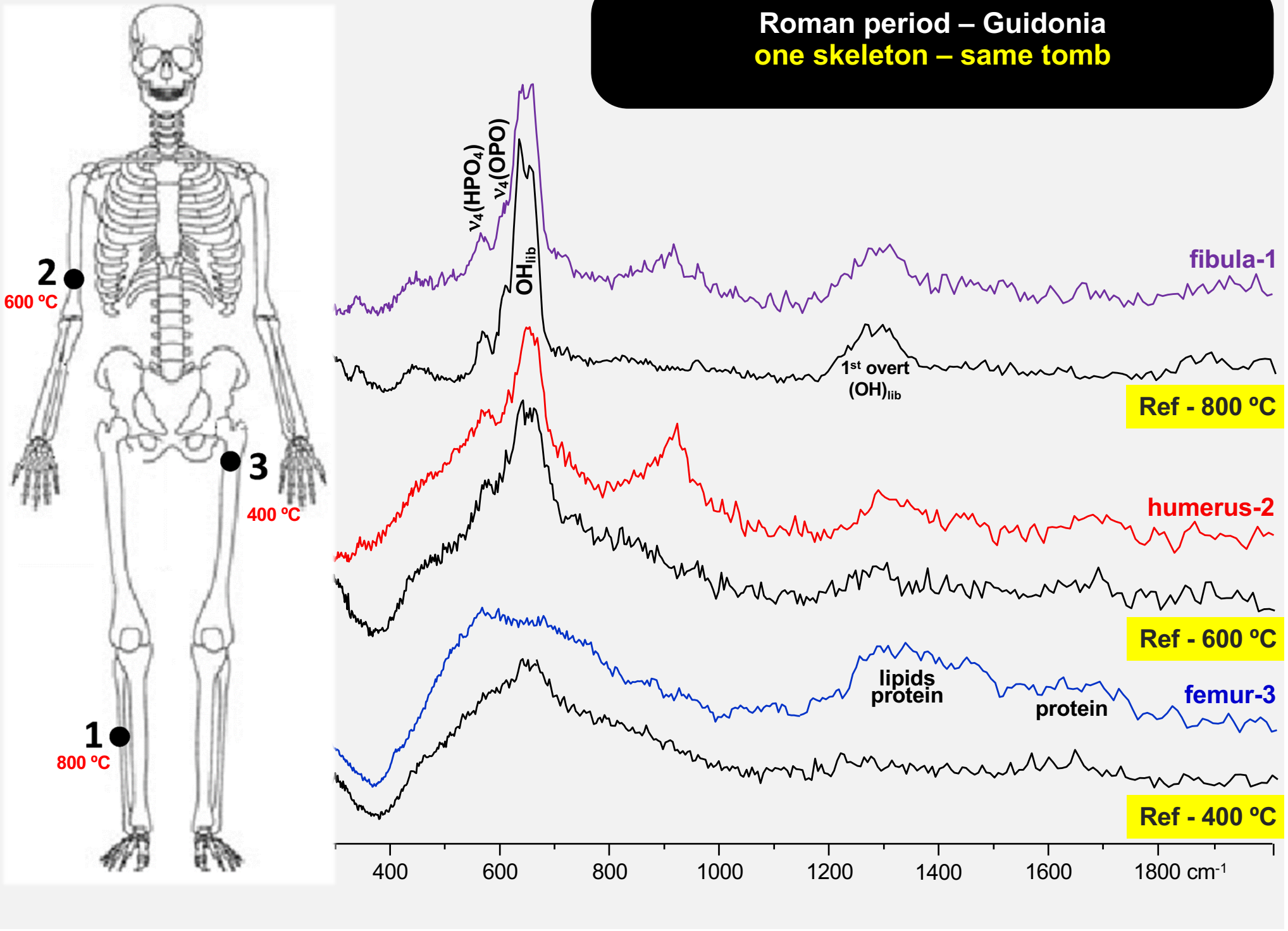
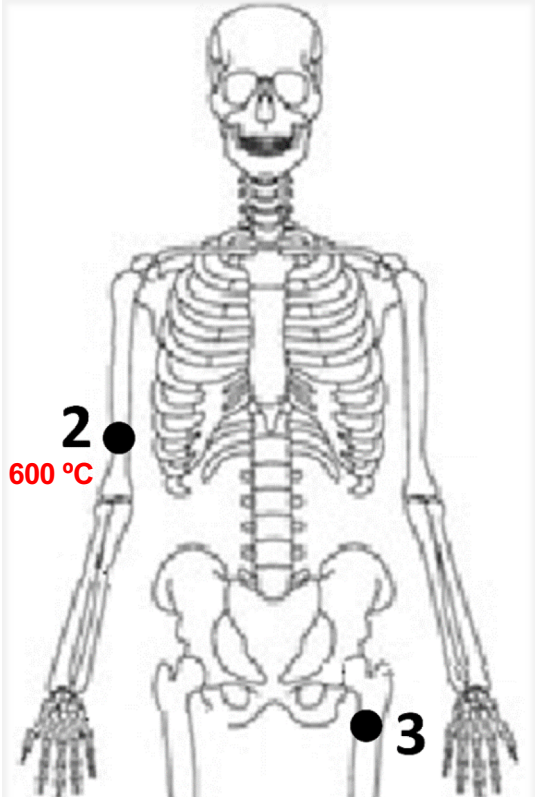
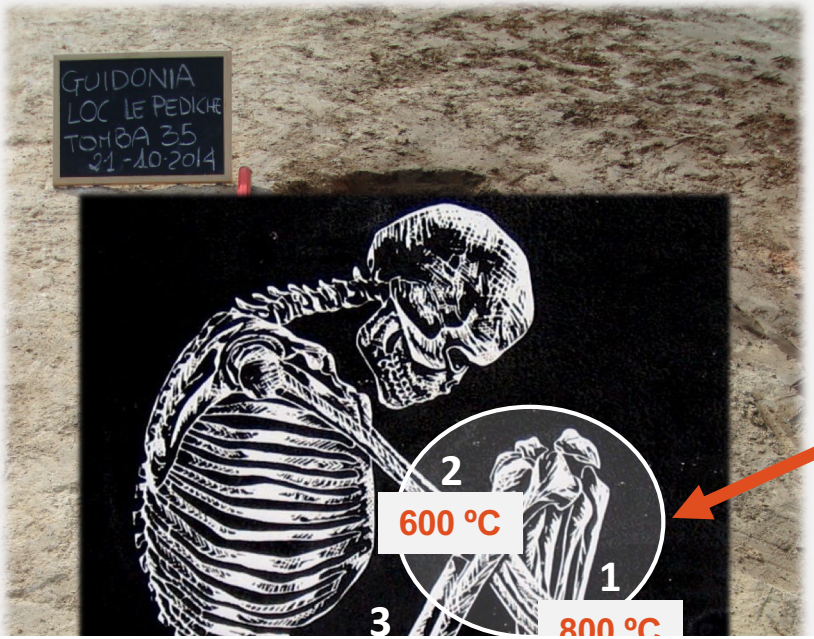

Roman period – Guidonia
one skeleton – same tomb
2
600 ºC
3
400 ºC
1
800 ºC
$\nu_4(HPO_4)$
$\nu_4(OPO)$
OH_{lib}
fibula-1
1st overt
$(OH)_{lib}$
Ref - 800 ºC
humerus-2
Ref - 600 ºC
lipids
protein
protein
femur-3
Ref - 400 ºC
400
600
800
1000
1200
1400
1600
1800 cm-1





just one skeleton

foetal position

burned inside the grave

from right to left

SCIENCE ADVANCES | RESEARCH ARTICLE

APPLIED SCIENCES AND ENGINEERING

First analysis of ancient burned human skeletal remains probed by neutron and optical vibrational spectroscopy

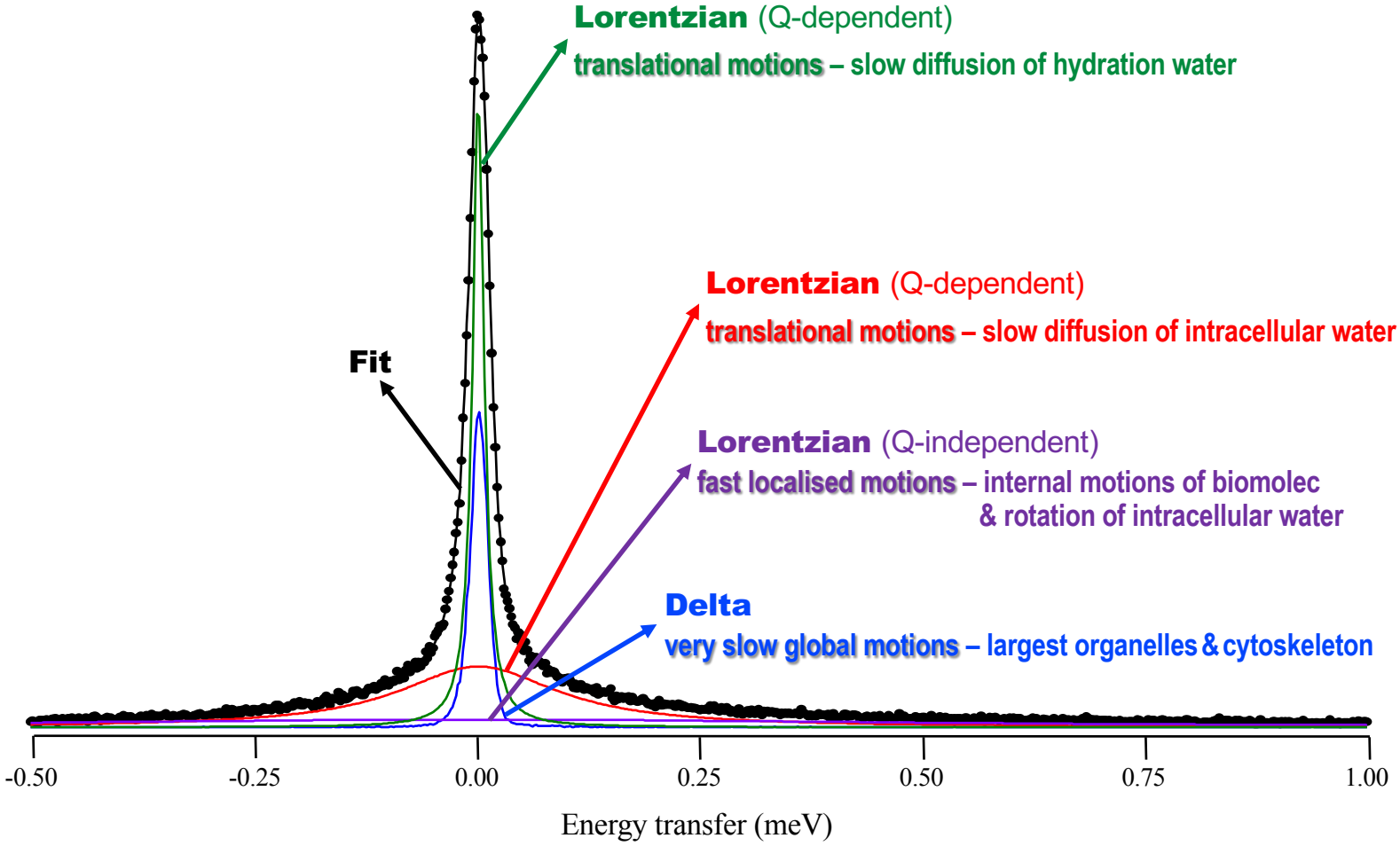
G. Festa[1]*, C. Andreani[1,2,3], M. Baldoni[4,5], V. Cipollari[6], C. Martínez-Labarga[3,4], F. Martini[7], O. Rickards[3,4], M. F. Rolfo[8], L. Sarti[9], N. Volante[9], R. Senesi[1,2,3], F. R. Stasolla[10], S. F. Parker[11], A. R. Vassalo[12], A. P. Mamede[12], L. A. E. Batista de Carvalho[12], M. P. M. Marques[12,13]


Obrigada

fitting QENS data

to represent several dynamic componentes within the cell

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



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Reference collection of human skeletons

samples burned under controlled conditions

400 to 1150 ºC (combustio n)

Lab Forensic Anthropology – Univ Coimbra (Portugal)

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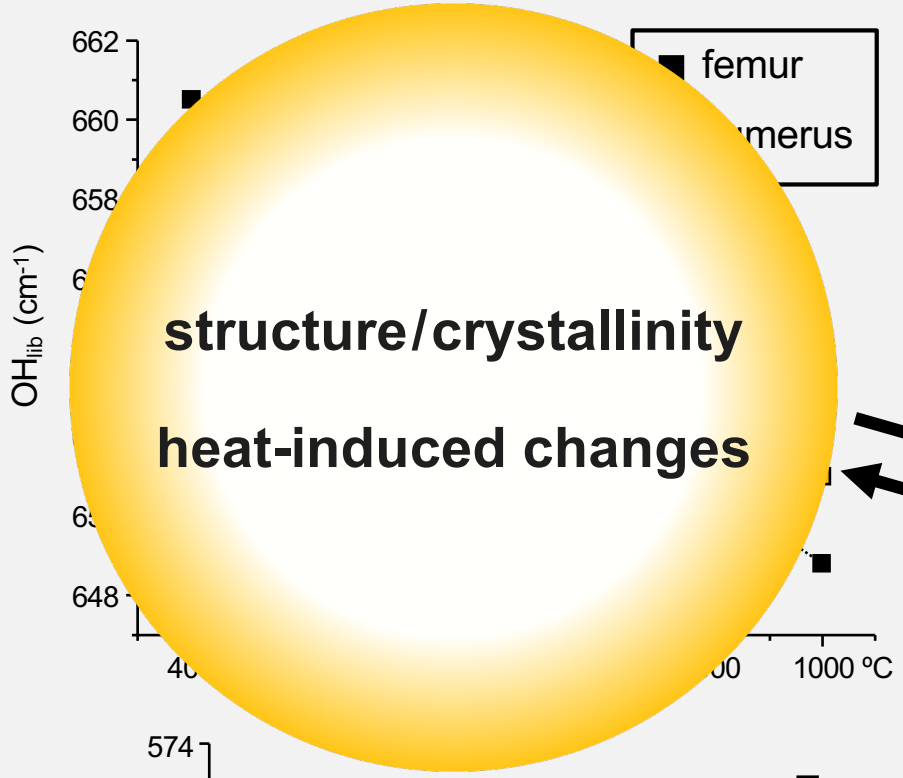
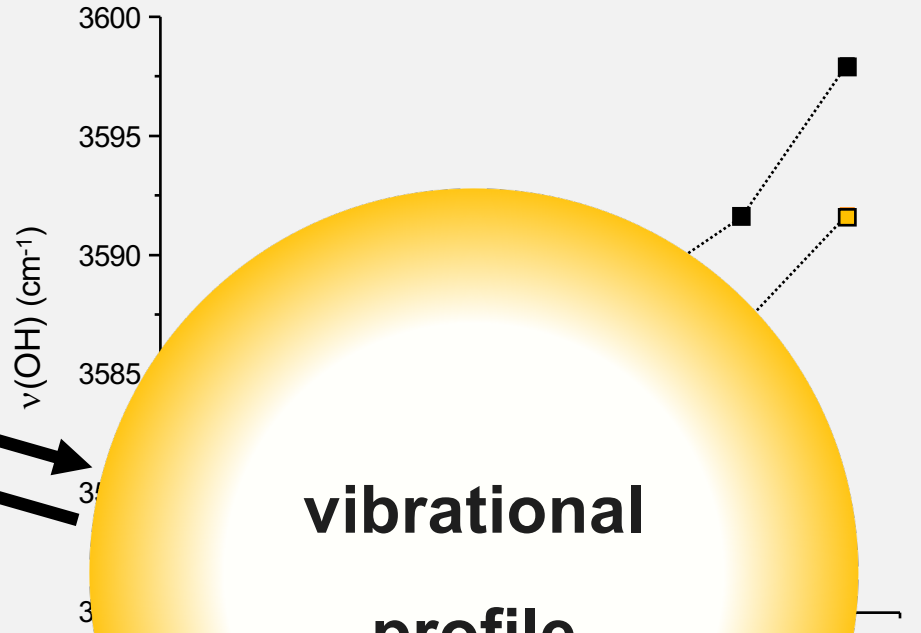
quantitative relationships

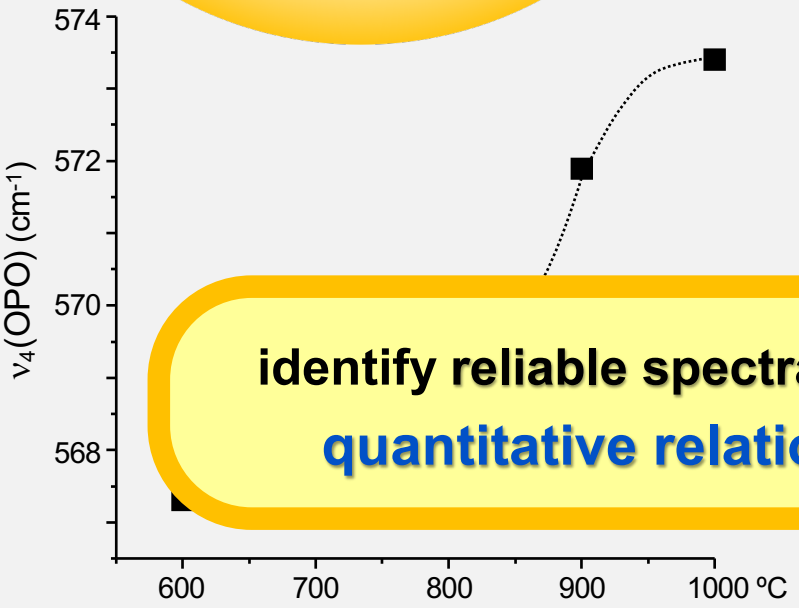


structure/crystallinity

heat-induced changes



vibrational profile



identify reliable spectral biomarkers for routine use

quantitative relationship ***unburn the bone***

Química-Física Molecular