School of Food Science and Nutrition
FACULTY OF MATHEMATICS AND PHYSICAL SCIENCES
UNIVERSITY OF LEEDS

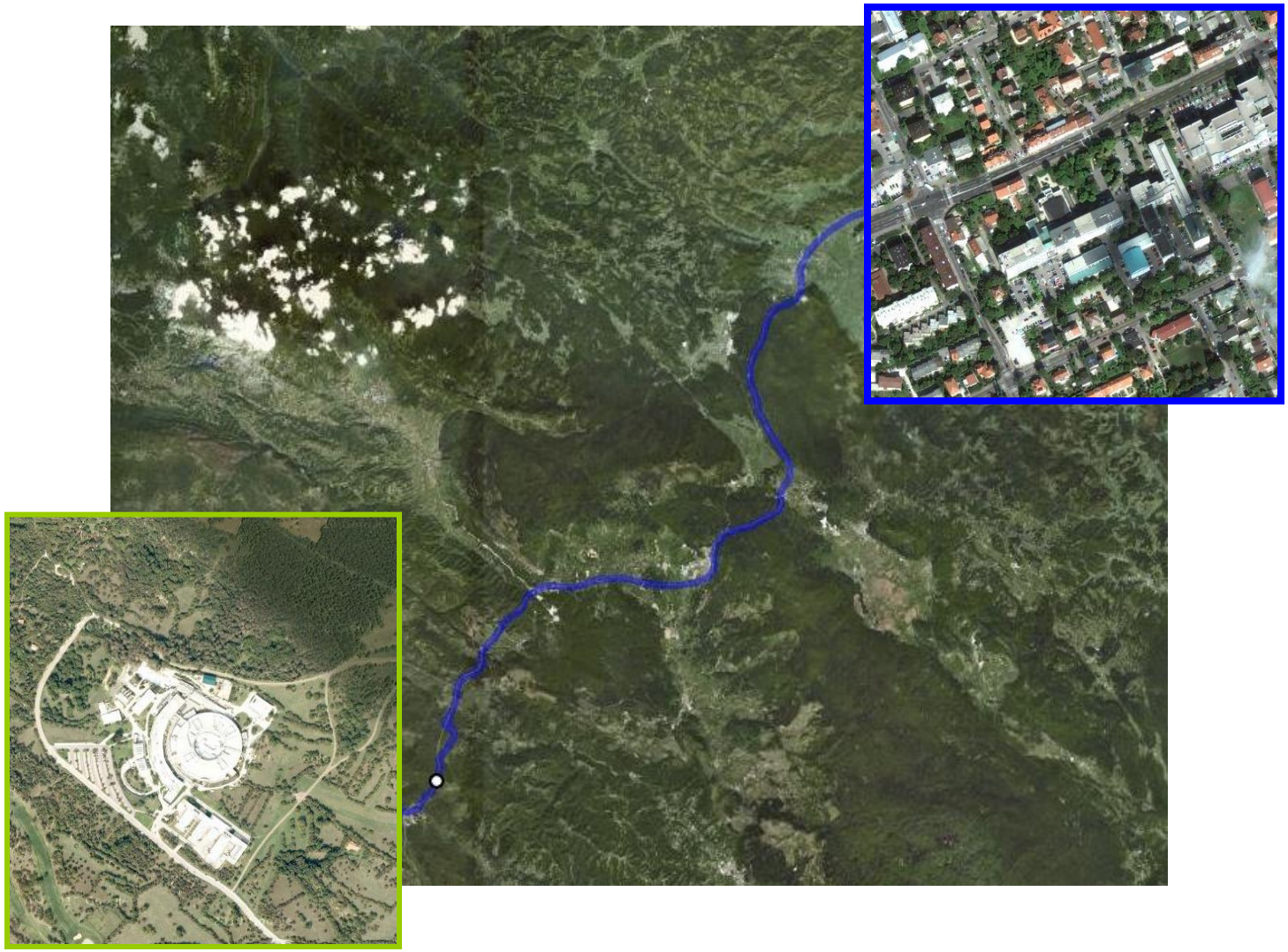
# Working at a Synchrotron

## Part 1

*Michael Rappolt*

*3. BSc Student Lecture: Physics with Introduction to Modern Physics*
5th of June 2014, Faculty of Electrical Engineering, University of Ljubljana

# Ljubljana – Trieste (Trst)



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# Some impressions from ELETTRA

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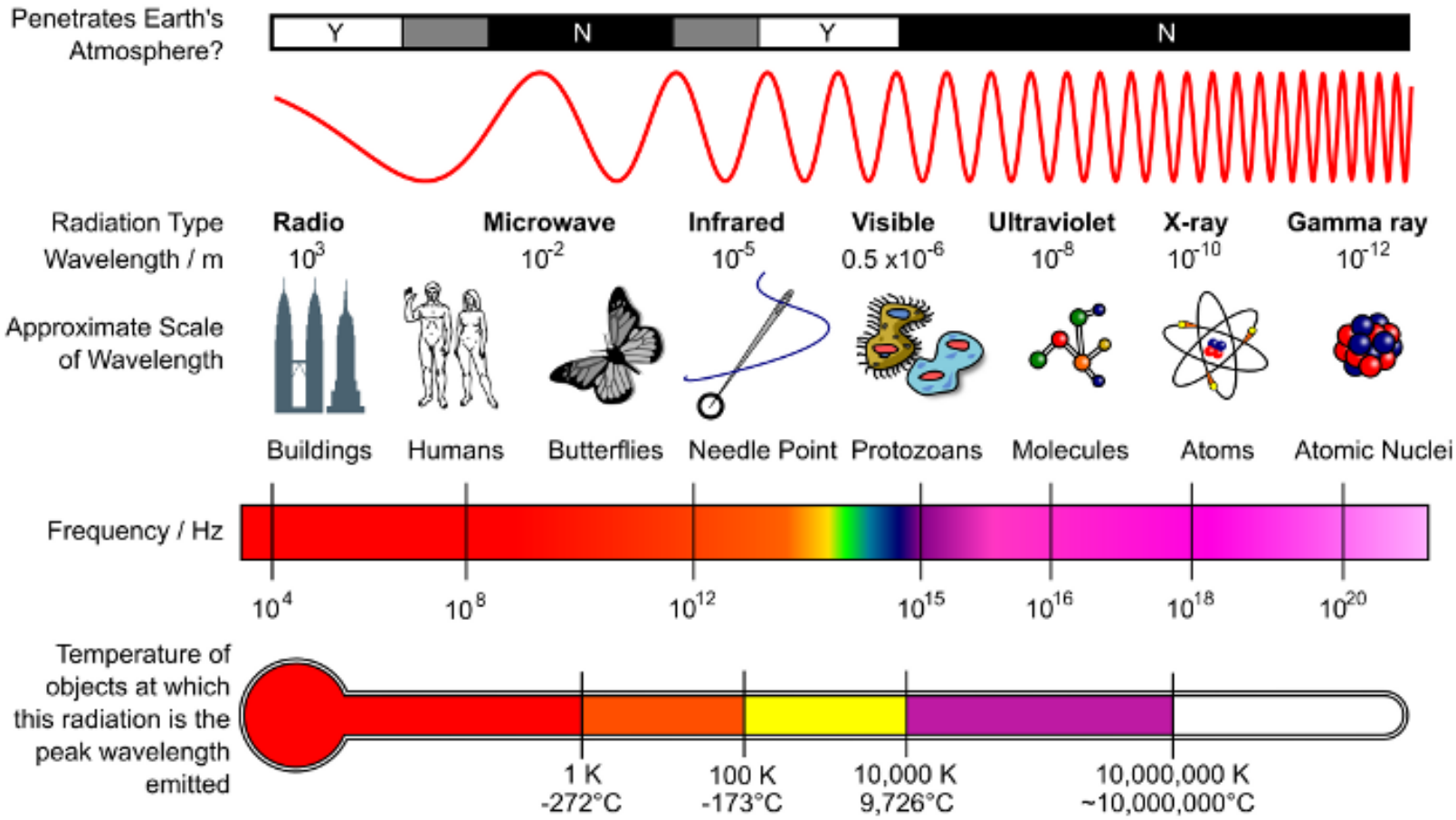
# Synchrotrons are Light Sources!

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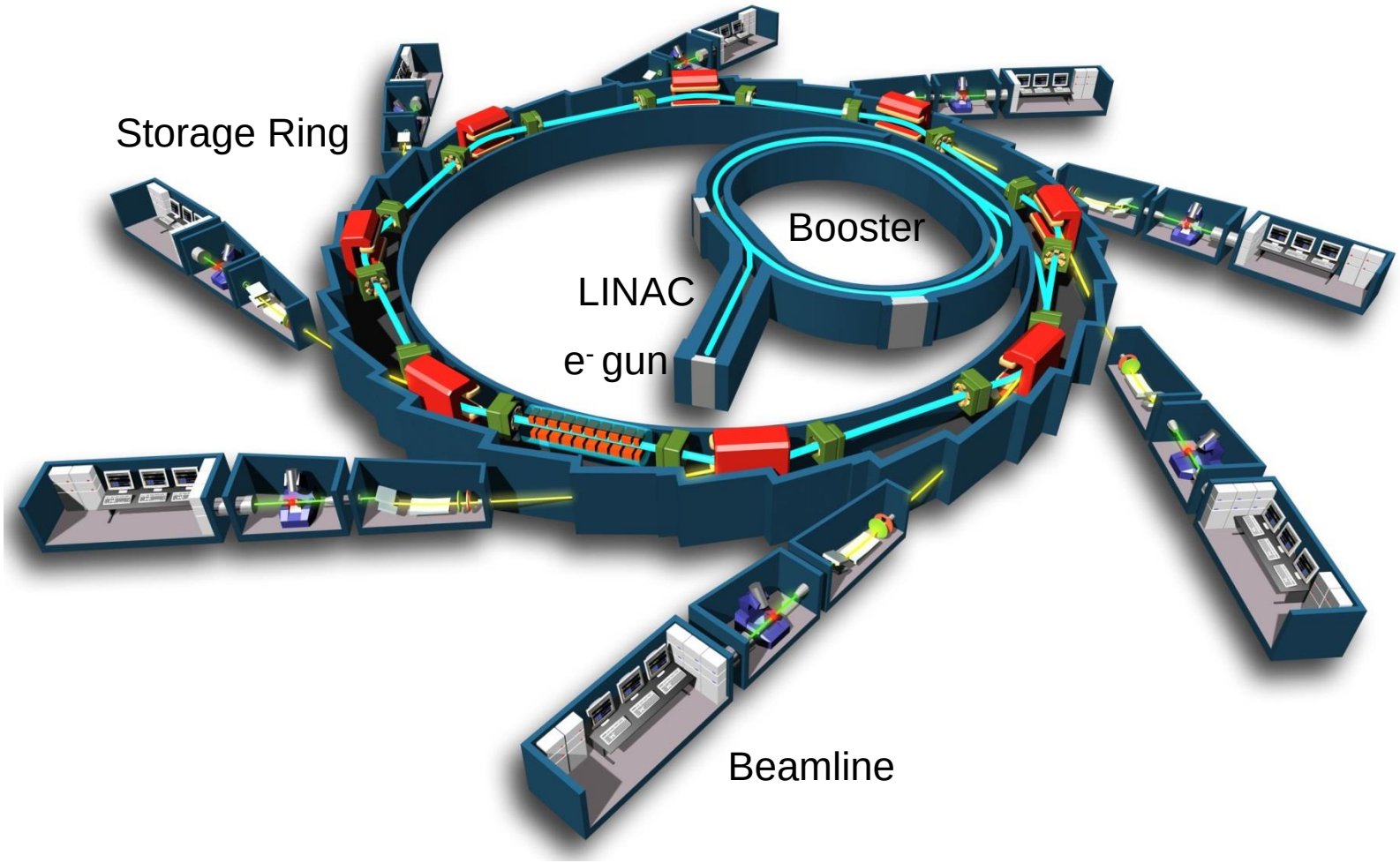
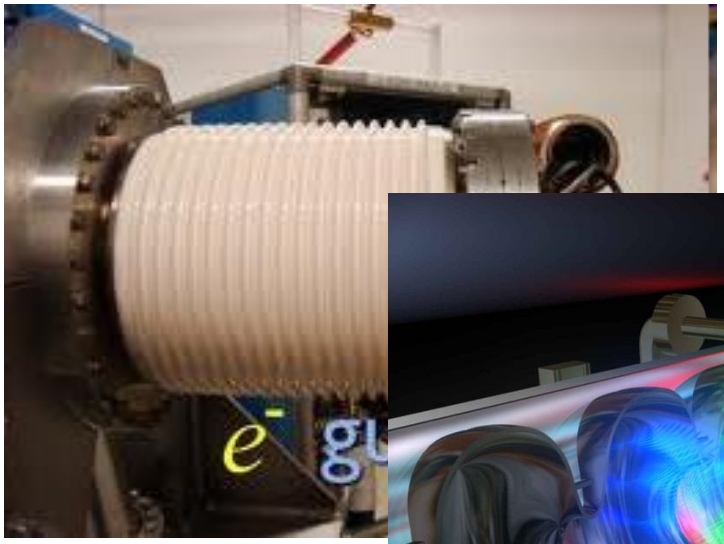
# Synchrotron Model

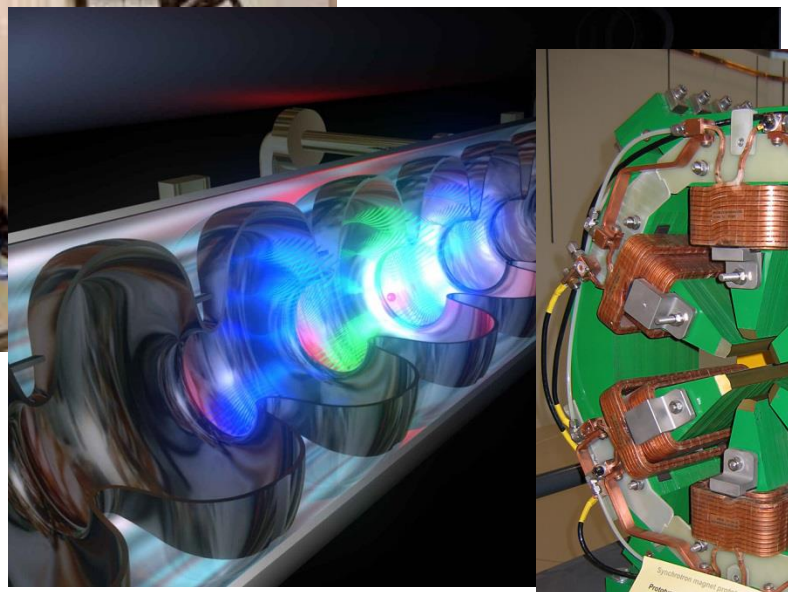


# Tracking the Electron Bunches



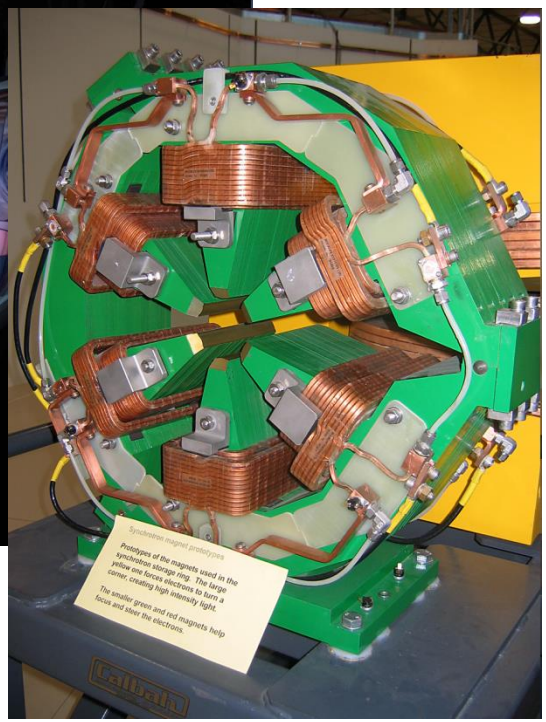

creation

thermionic emission from a heated metal cathode



acceleration

radio frequency acceleration cavity




focusing

quadro-, sexto- and octopol magnets

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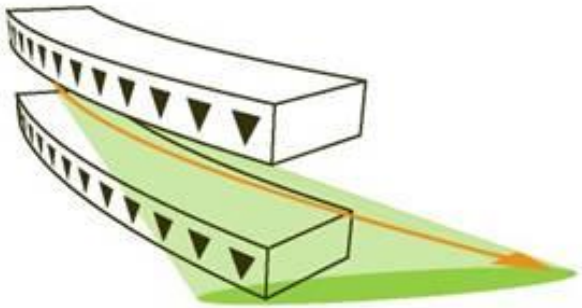
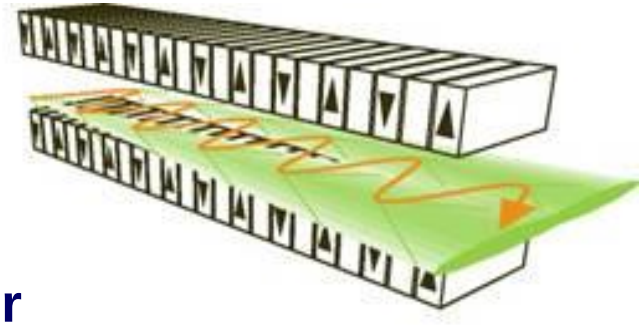
# Types of Light Sources



**Bending magnet -** sweeping searchlight

At each deflection of the electron path a beam of radiation is produced.

Insertion devices - produce higher intensity



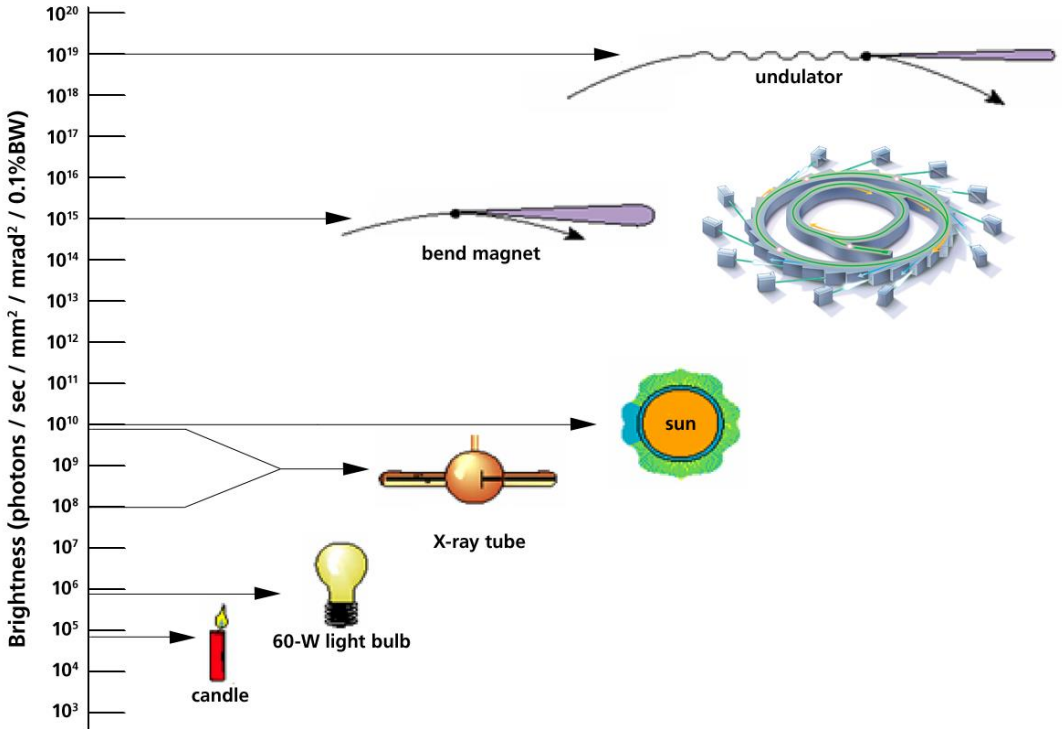
**Wiggler**

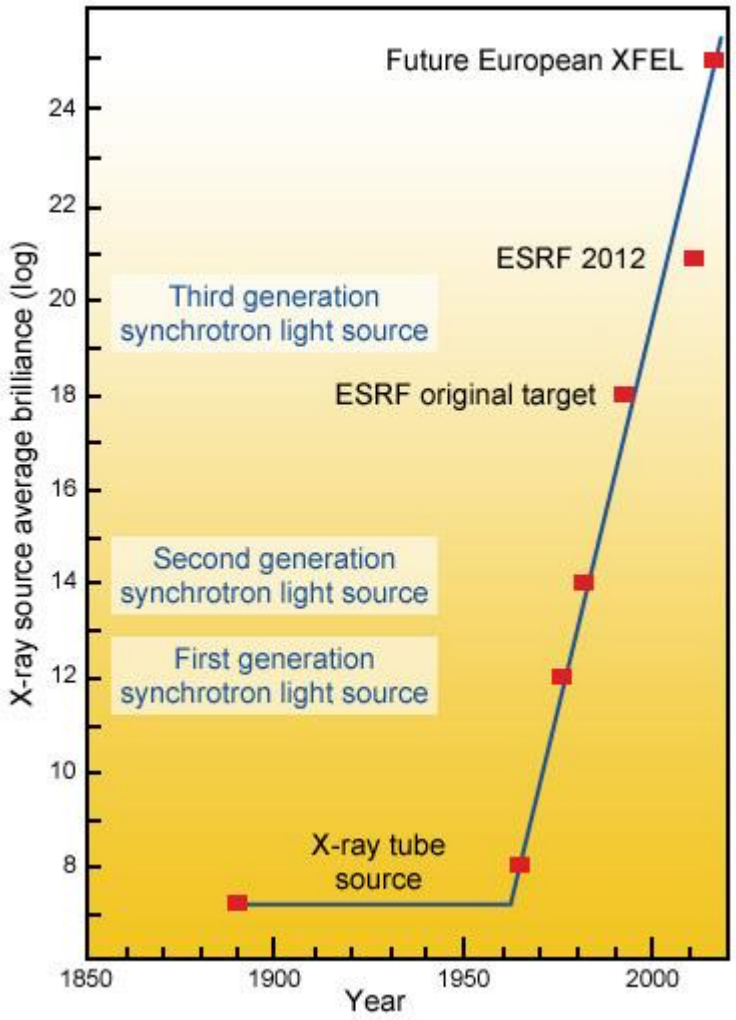
Beams emitted at each pole reinforce each other and appear as a broad beam of incoherent light.

**Undulator**

Produces a very narrow beam of coherent light, amplified by up to $10^4$

# Brilliance of Synchrotron Light

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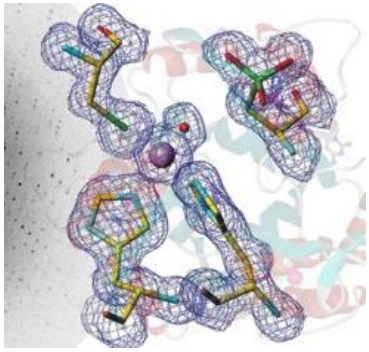
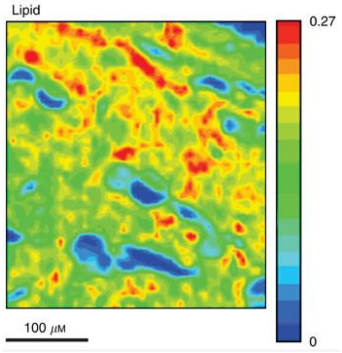
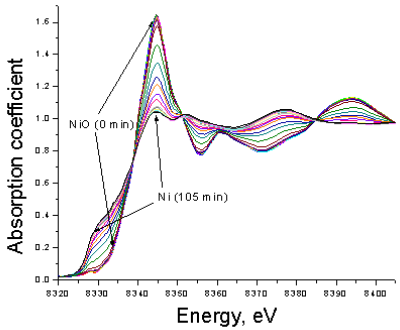
# Applied Techniques at ELETTRA for Biology and Medicine

- Diffraction: Protein crystallography
- Small Angle X-ray Scattering
- Absorption: EXAFS
- Infrared Spectroscopy & Microscopy
- TwinMic
- Imaging: Tomography & Mammography



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# Beamlines at ELETTRA: XRD

*Protein Crystallography

## Contacts


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**Doriano Lamba**
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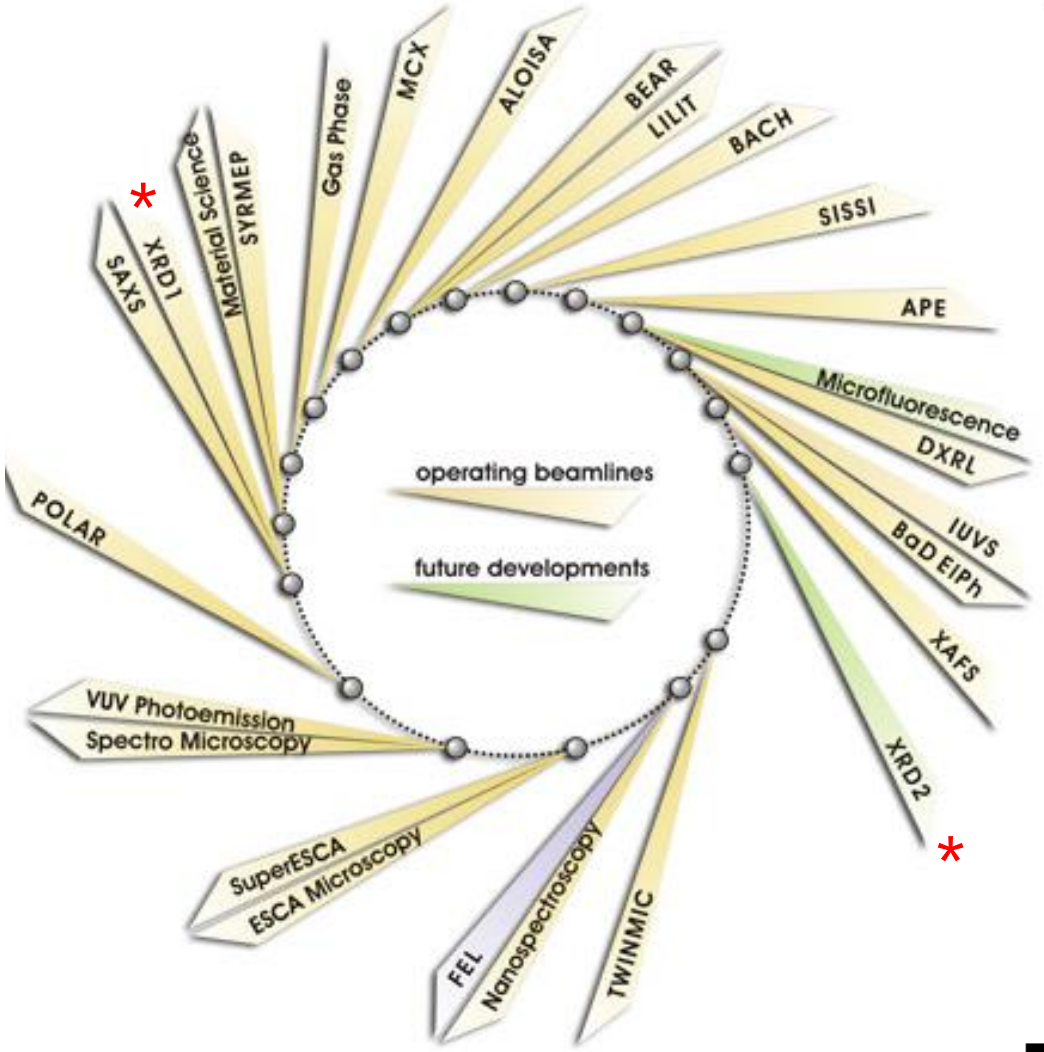
*tel.* +39.040.375.8514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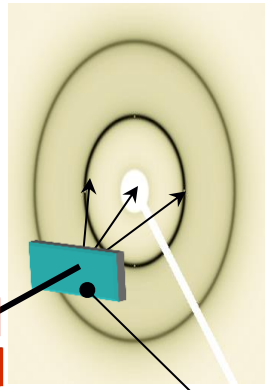
# Scheme of a X-ray Scattering (Diffraction) Beamline


Cooled Crystal Set

X-ray pattern



3. collimation system

sample

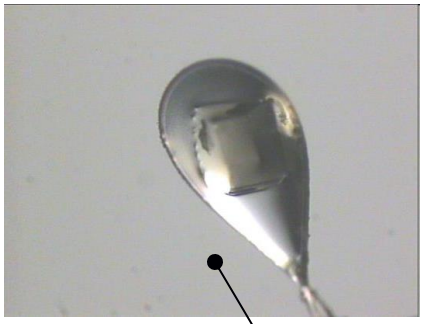
1. monochromator

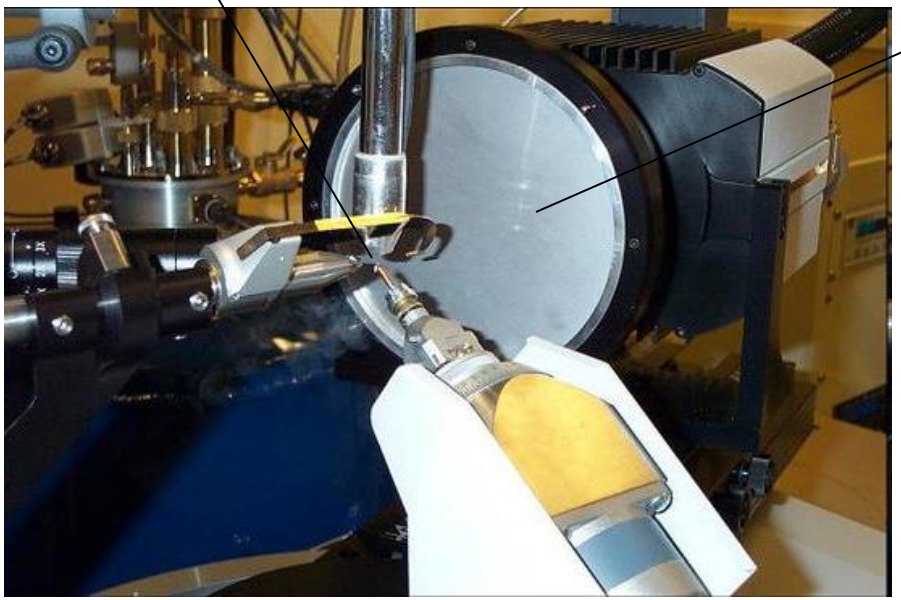
2. toroidal mirror

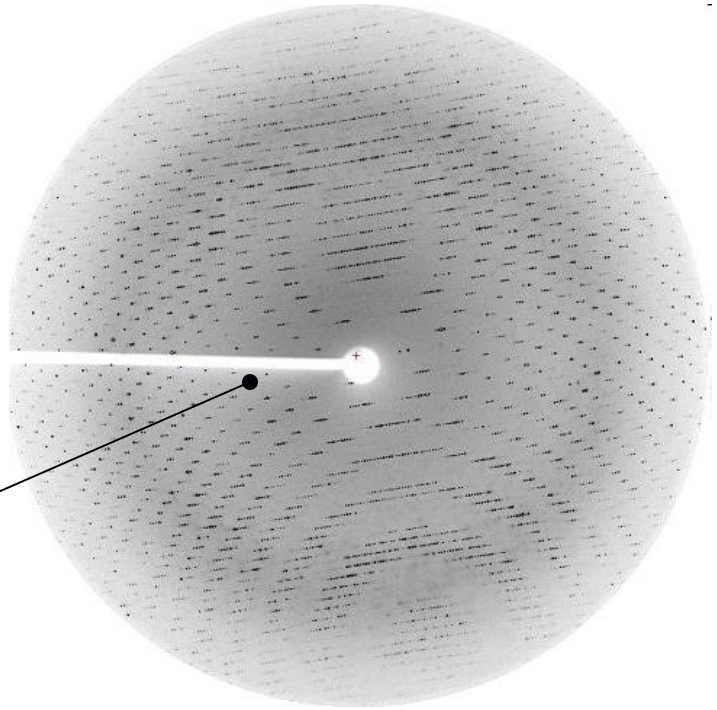
synchrotron light


Toroidal Mirror

# Protein Crystallography Set-up







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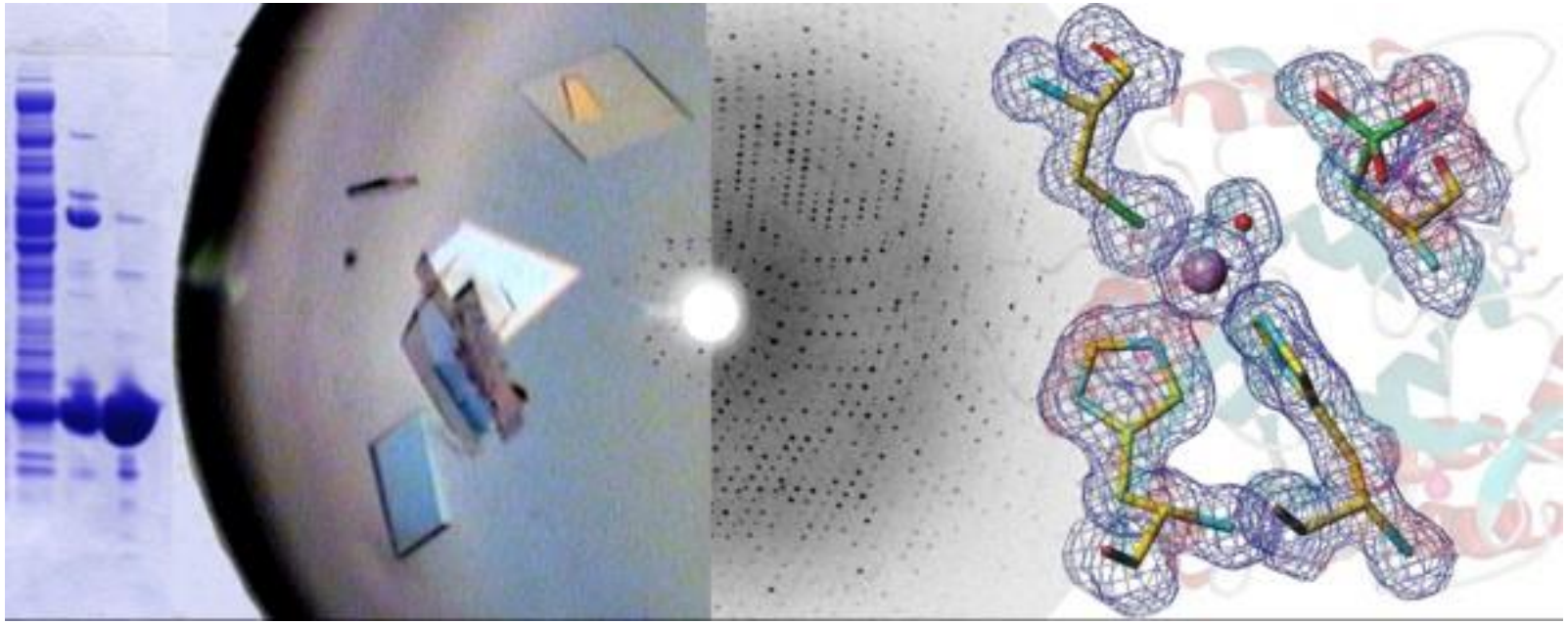
# Protein Crystallography: Different Working Steps



1. Purification

2. Protein Crystallization

3. X-ray Diffraction

4. Electron Density Determination

# Protein Structure, e.g. Ribosome

Chemistry

## The Nobel Prize in Chemistry 2009

"for studies of the structure and function of the ribosome"

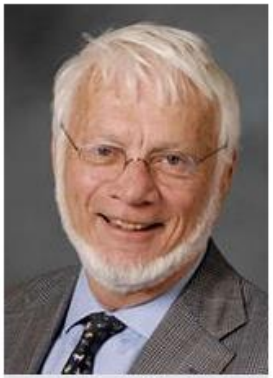
Photo: MRC Laboratory of Molecular Biology

**Venkatraman Ramakrishnan**

1/3 of the prize

United Kingdom

MRC Laboratory of Molecular Biology
Cambridge, United Kingdom



Credits: Michael Marsland/Yale University

**Thomas A. Steitz**

1/3 of the prize

USA

Yale University
New Haven, CT, USA;
Howard Hughes Medical Institute

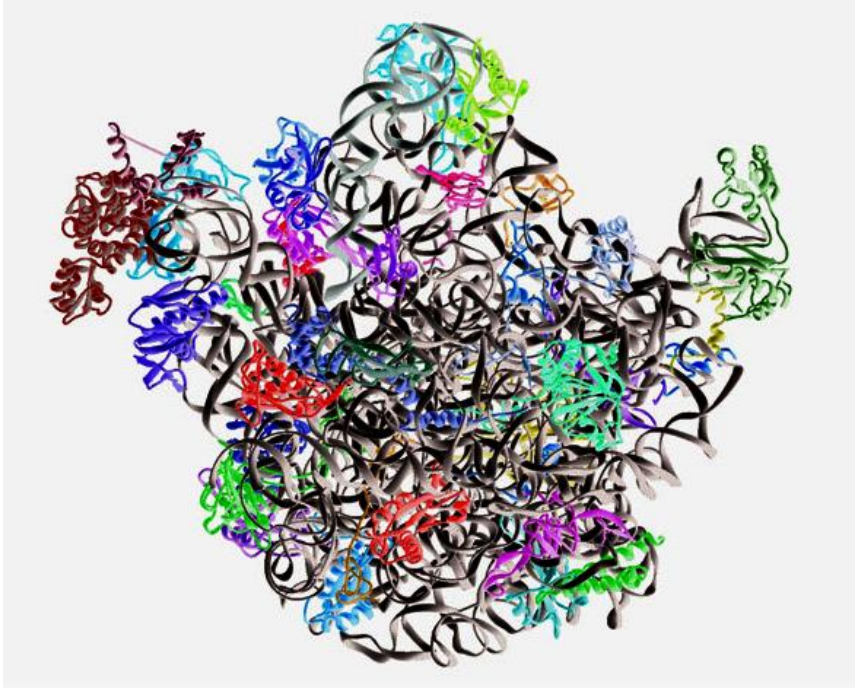
Credits: Micheline Pelletier/Corbis

**Ada E. Yonath**

1/3 of the prize

Israel

Weizmann Institute of Science
Rehovot, Israel



More than 20 years of work are in this stucture!

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# Beamlines at ELETTRA: SAXS

*Small Angle X-ray Scattering

Contacts


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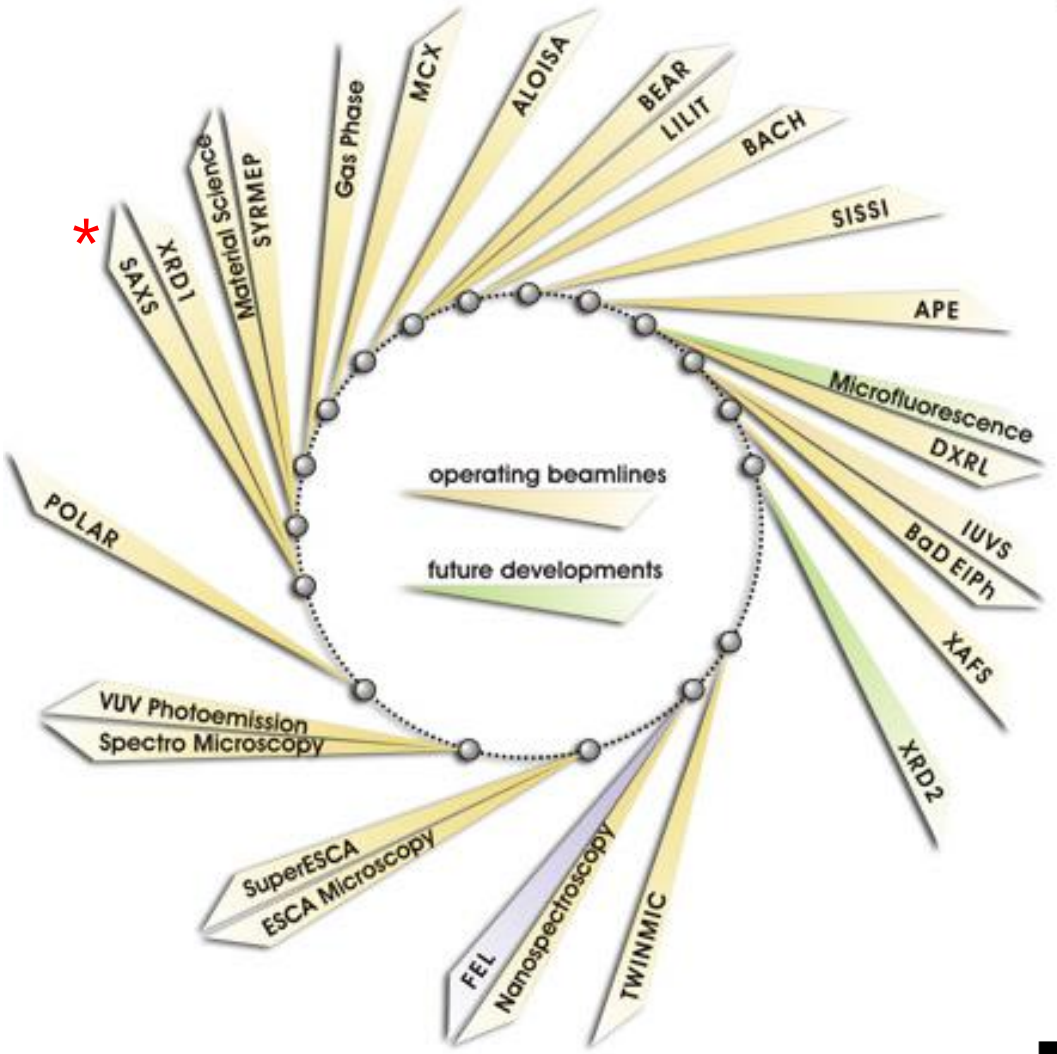
*tel:* + 39 040 375 8572
*fax:* + 39 040 9380 902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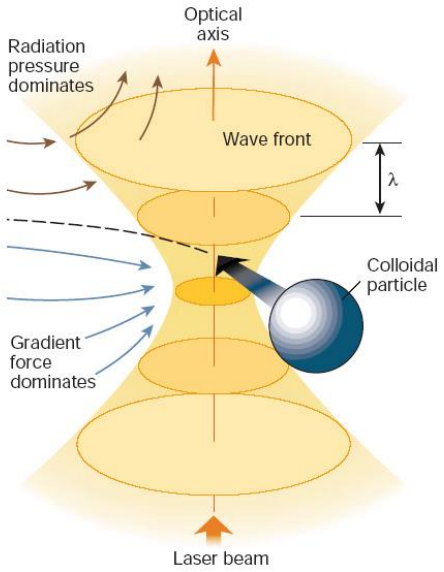
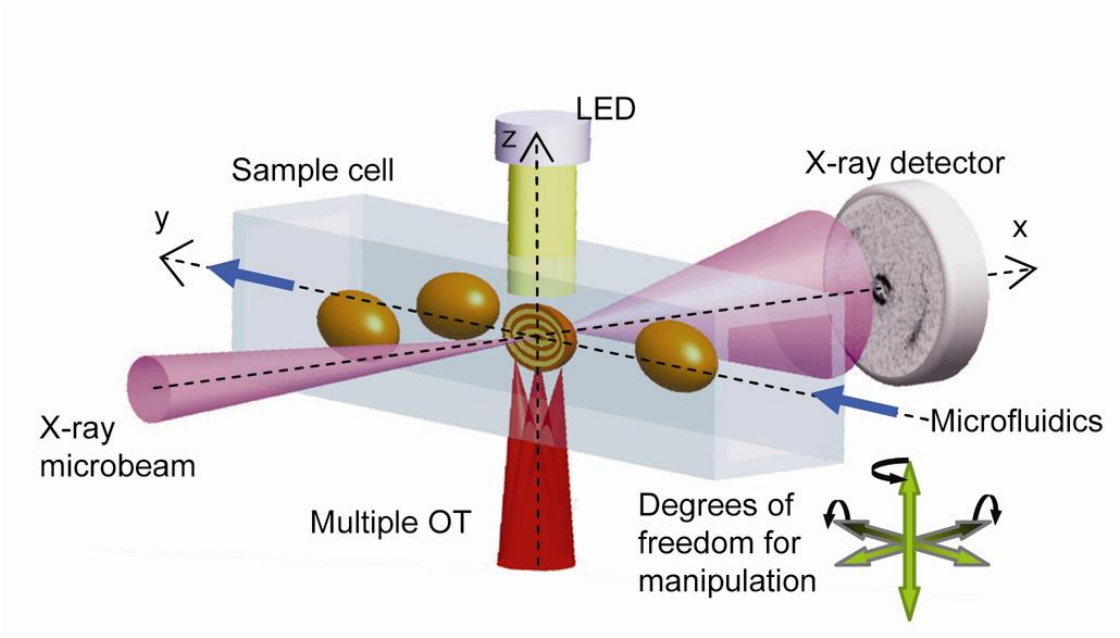
# Make the Impossible Possible!




Grier, Nature **24**, 810 (2003)

The narrowest point of the focused laser beam contains a strong **electric field gradient**.

Dielectric particles are attracted along the gradient to the centre of the beam.




Cojoc..Rappolt et al. Applied Physics Letters 91 (**2007**)
Cojoc.. Rappolt et al. Applied Physics Letters 97 (**2010**)

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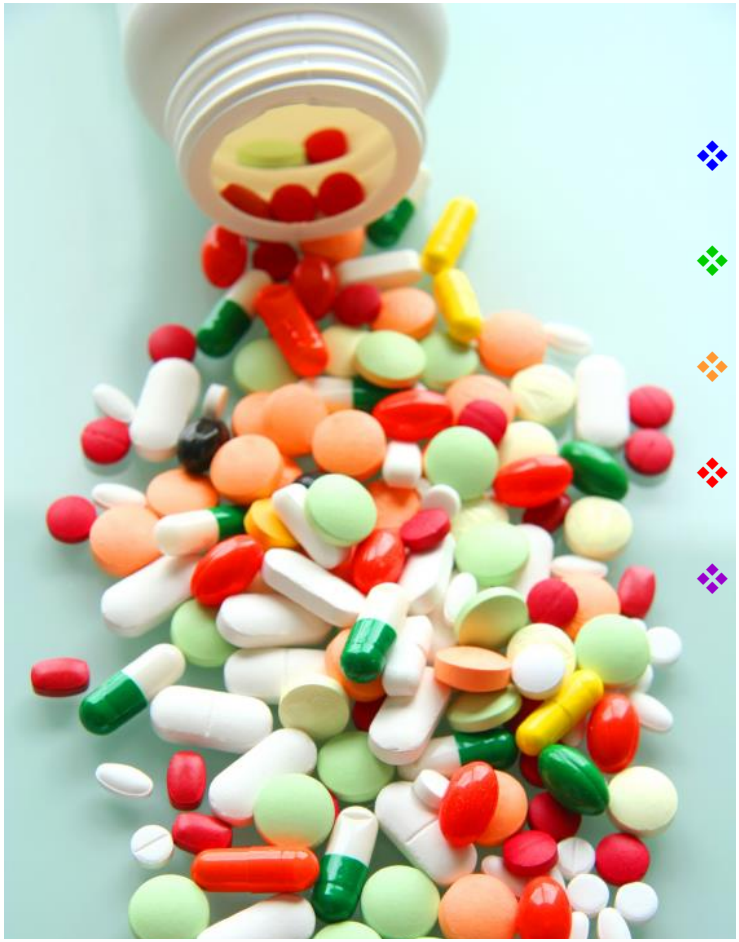
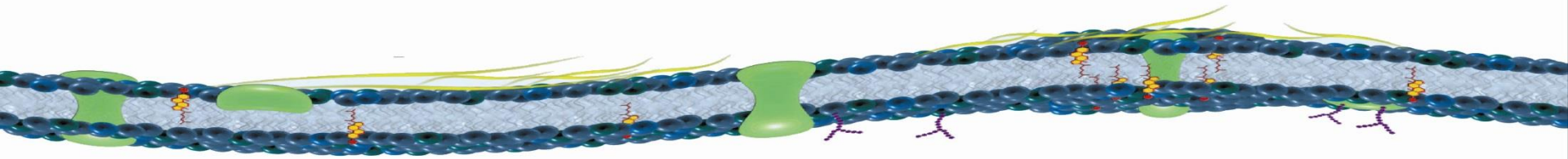
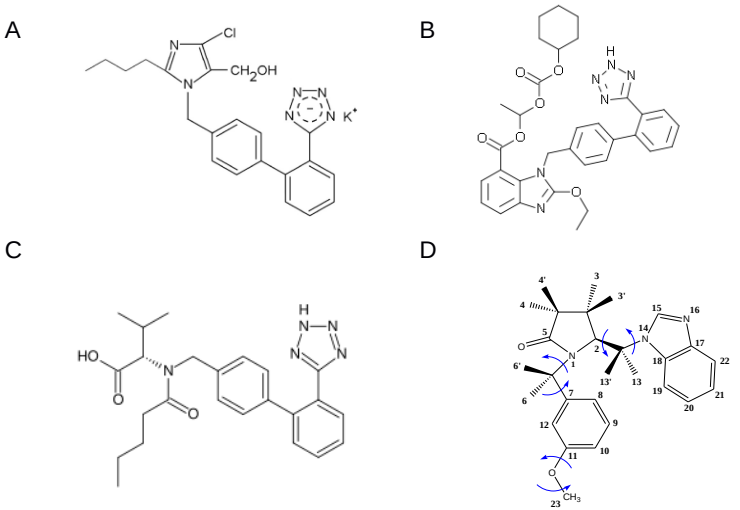
# Fields of Application in Membrane Research



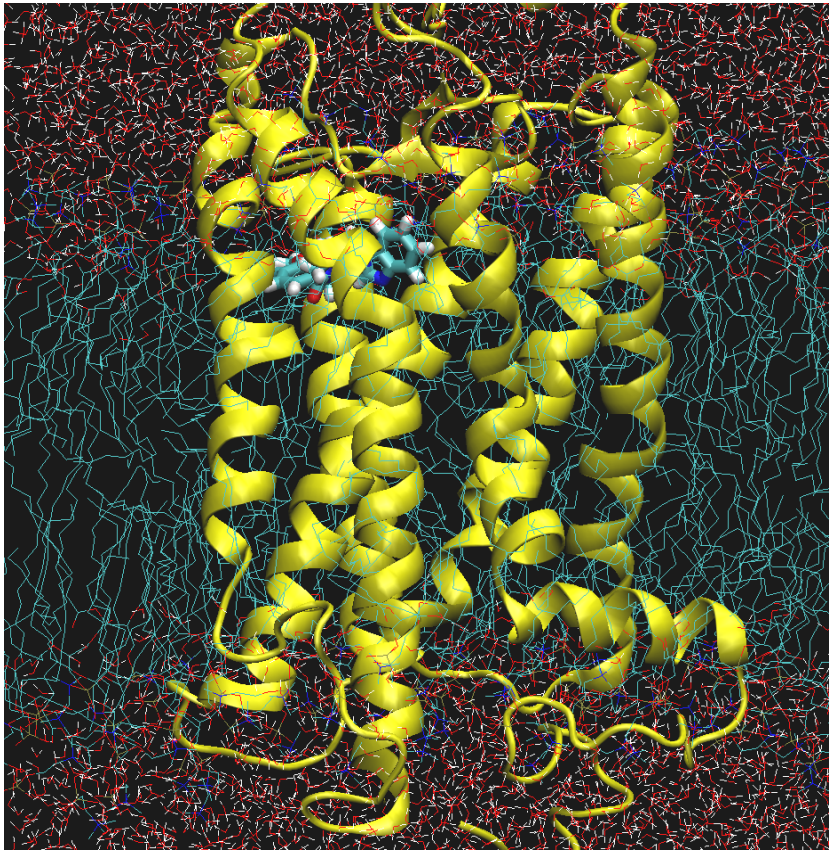
- Medicine: Antihypertensive drugs (ARBs)
- Biology: Mediated protein function
- Drug delivery: Light activated vesicles
- Nanotechnology: Cubosomes and hexosomes
- Food Science: The role *trans*-fatty acids



# Interactions of Different Sartans with the Bilayer Interface




Chemical structures of losartan-potassium (A), candersartan-cilexetil (B), valsartan (C), and MMK3 (D).



Docking of MMK3 in $AT_1$ receptor surrounded by lipid bilayers. Yellow color represents the seven helices of $AT_1$ receptor. Figure taken from:

C. Fotakis, S. Gega, E. Siapi, C. Potamitis, K. Viras, P. Moutevelis-Minakakis, C.G. Kokotos, S. Durdagi, S. Golic Grdadolnik , B. Sartori, M. Rappolt, and T. Mavromoustakos (2010) *BBA-Membranes* **1768**,422-432.

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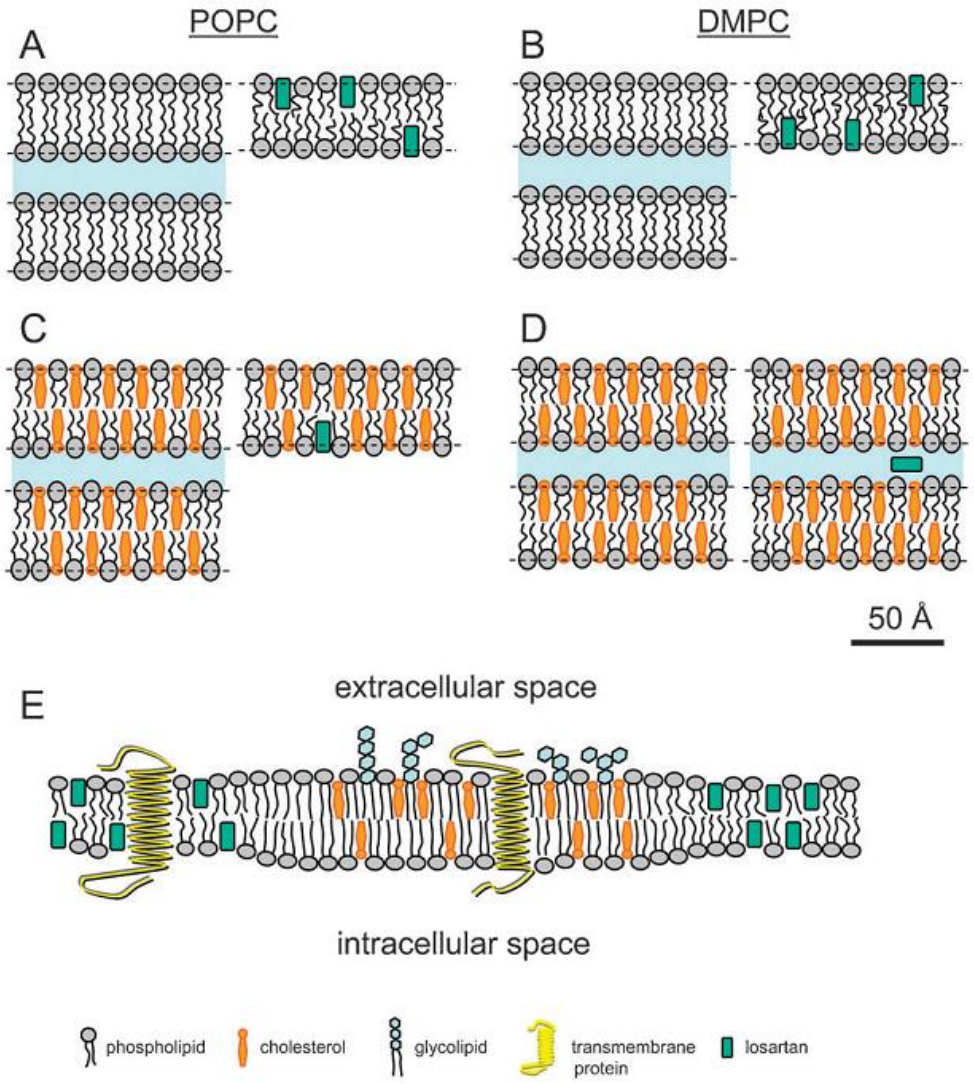
# Interactions of Different Sartans with the Bilayer Interface (II)



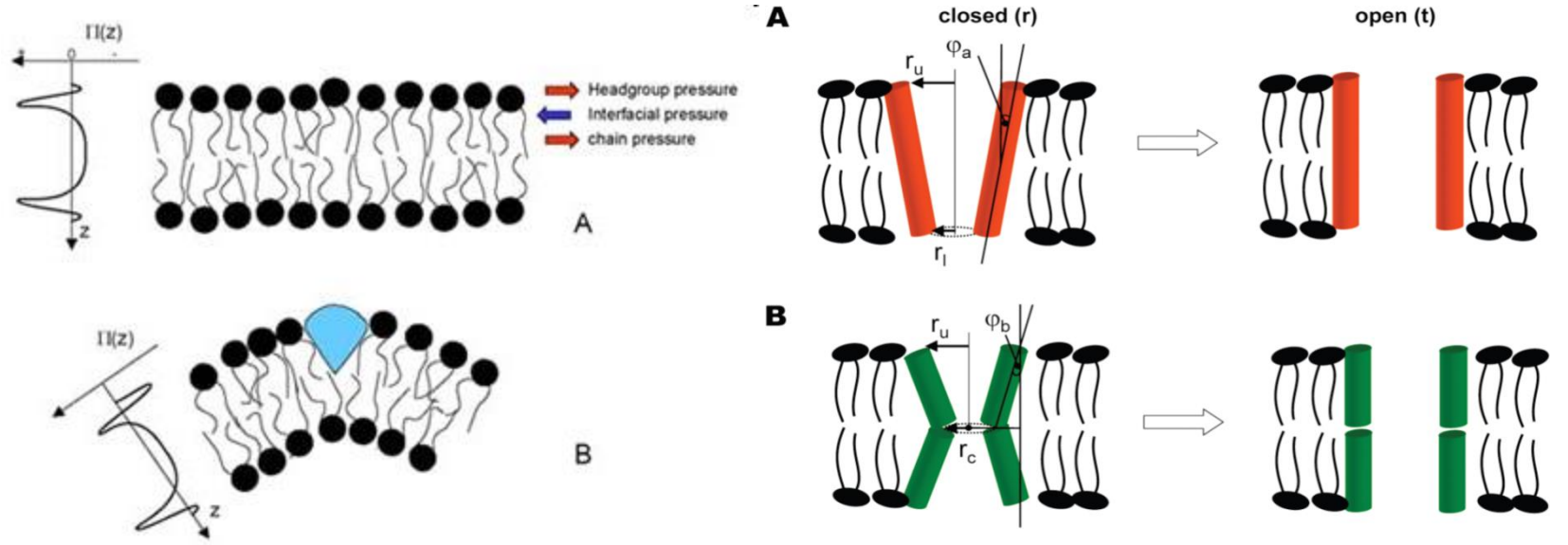

## Results

- Membrane thinning
- Area/molecule decrease
- Losartan is avoiding the raft

Hodzic, A., Zoumpoulakis, P., Pabst G., Mavromostakos, T., and Rappolt, M. (2012):

Losartan‘s affinity to fluid bilayers modulates lipid/cholesterol interaction. PCCP 14: 4780-4788.

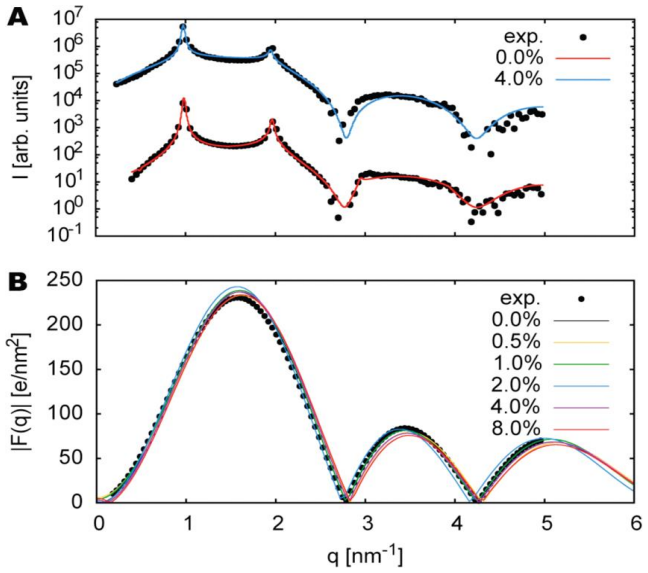
# Hypothesis of Cantor: Membrane Mediated Protein Function

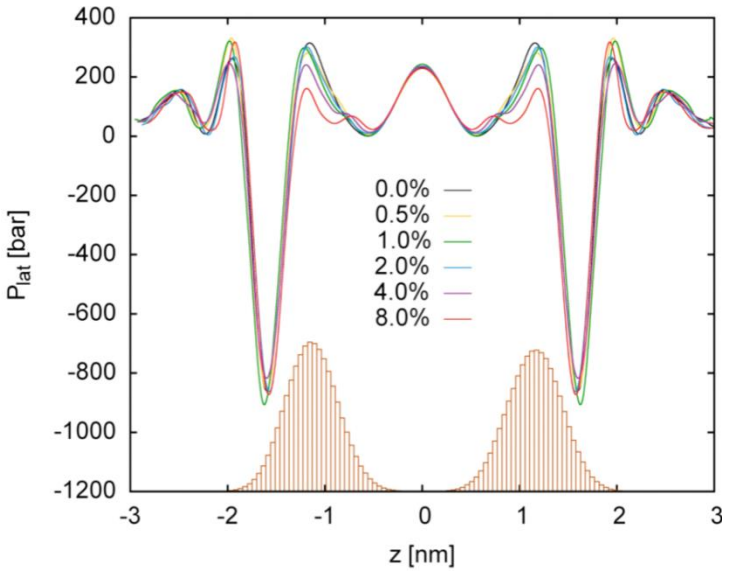



**Hypothesis of Cantor***: Changes in the lateral pressure profile as a function of the depth z can induce conformational changes in membran proteins.

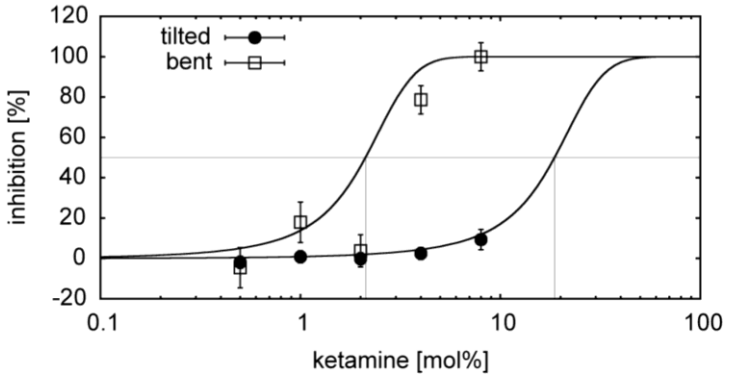
Cantor, S. R. *Biochemistry* **1997**, *36*, 2339–2344.

# Membrane-Mediated Effect on Ion Channels Induced by the Anesthetic Drug Ketamine




Estimation of the percent inhibition. IC50 values for the two channel models are indicated by a gray line




Figures taken from:

Jerabek, H., G. Pabst, M. Rappolt & T. Stockner (2010) Membrane-mediated effect on ion channels induced by the anesthetic drug ketamine. *J. Am. Chem. Soc.* **132**: 7990 - 7997 (2010)

# Light Induced Controlled Release from Vesicles

THE JOURNAL OF PHYSICAL CHEMISTRY Letters

2010

pubs.acs.org/JPCL

## Structural Elucidation of Light Activated Vesicles

Anan Yaghmur,*,† Lauri Paasonen,†,§ Marjo Yliperttula,§ Arto Urtti,† and Michael Rappolt*,∥

†Faculty of Pharmaceutical Sciences, Department of Pharmaceutics and Analytical Chemistry, University of Copenhagen, Copenhagen, Denmark, ‡Centre for Drug Research, University of Helsinki, Helsinki, Finland, §Division of Biopharmacy and Pharmacokinetics, Faculty of Pharmacy, University of Helsinki, Helsinki, Finland, and ∥Institute of Biophysics and Nanosystems Research (IBN), Austrian Academy of Sciences, Graz, Austria

NANOMEDICINE

Journal of Controlled Release 147 (2010) 136–143

Contents lists available at ScienceDirect

Journal of Controlled Release

journal homepage: www.elsevier.com/locate/jconrel

## Gold-embedded photosensitive liposomes for drug delivery: Triggering mechanism and intracellular release

Lauri Paasonen [a,b], Tuomas Sipilä [b], Astrid Subrizi [a,b], Pasi Laurinmäki [e], Sarah J. Butcher [e], Michael Rappolt [c], Anan Yaghmur [d], Arto Urtti [a,*], Marjo Yliperttula [b]

[a] Centre for Drug Research, University of Helsinki, Helsinki, Finland
[b] Division of Biopharmacy and Pharmacokinetics, Faculty of Pharmacy, University of Helsinki, Helsinki, Finland
[c] Institute of Biophysics and Nanosystems Research, Austrian Academy of Sciences, c/o Sincrotrone Trieste, Italy
[d] Department of Pharmaceutics and Analytical Chemistry, Faculty of Pharmaceutical Sciences, University of Copenhagen, Copenhagen, Denmark
[e] Institute of Biotechnology and Department of Biosciences, University of Helsinki, Helsinki, Finland

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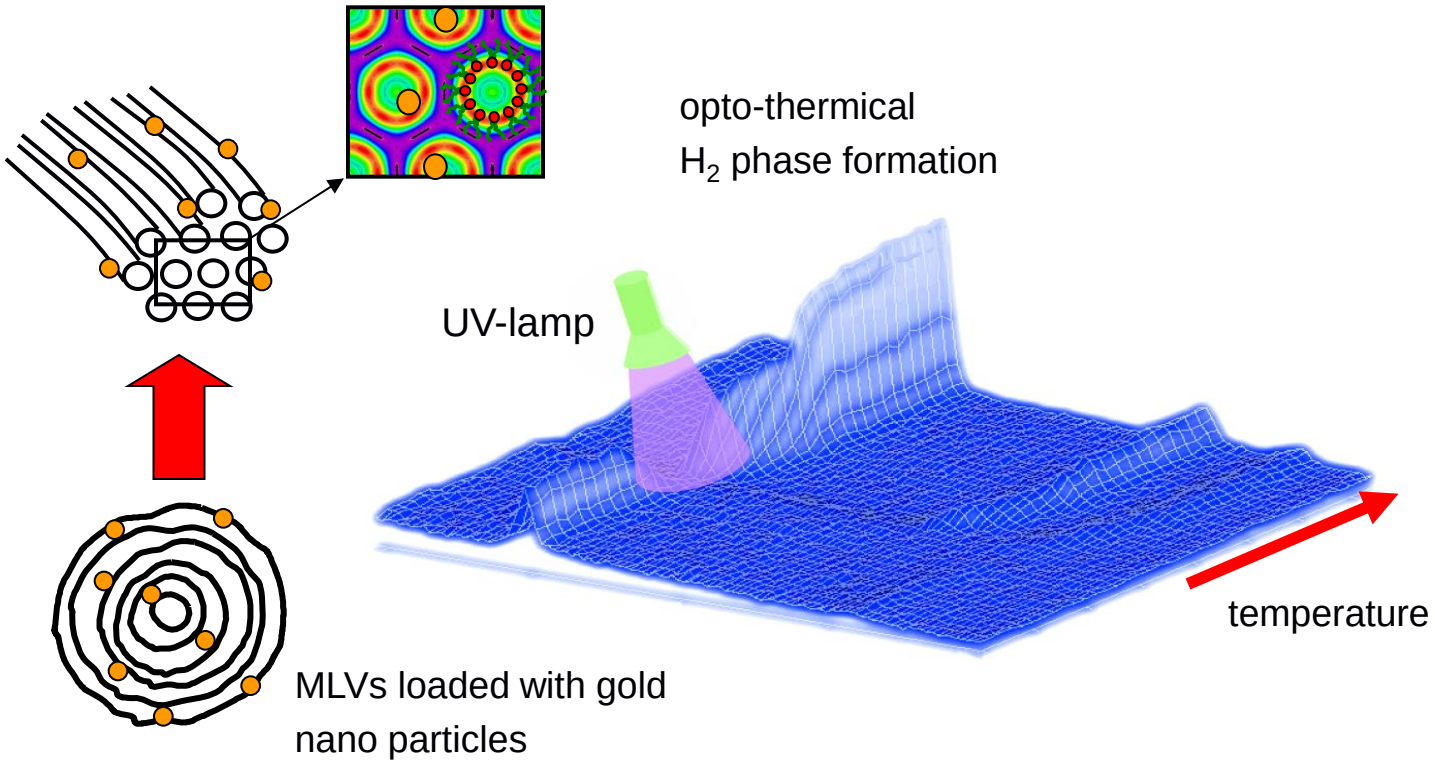
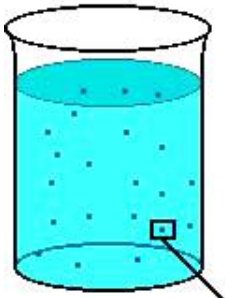
# Light Induced Phase Transition

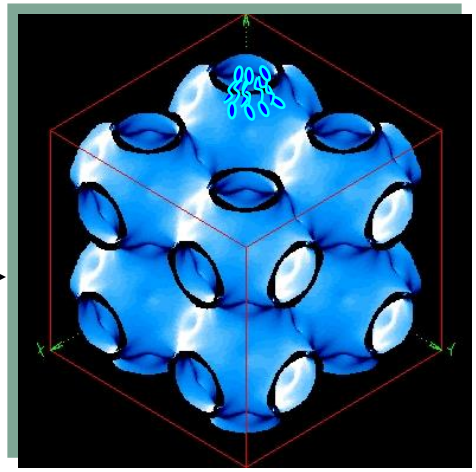


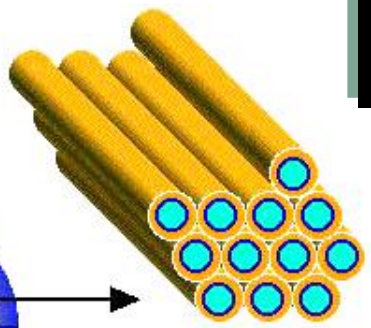
# Cubosomes & Hexosomes

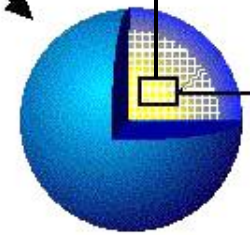
dispersion of „cubosomes“ or „hexosomes“

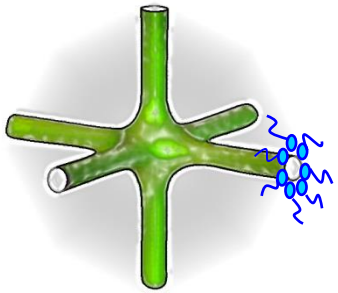


inner nanostructure









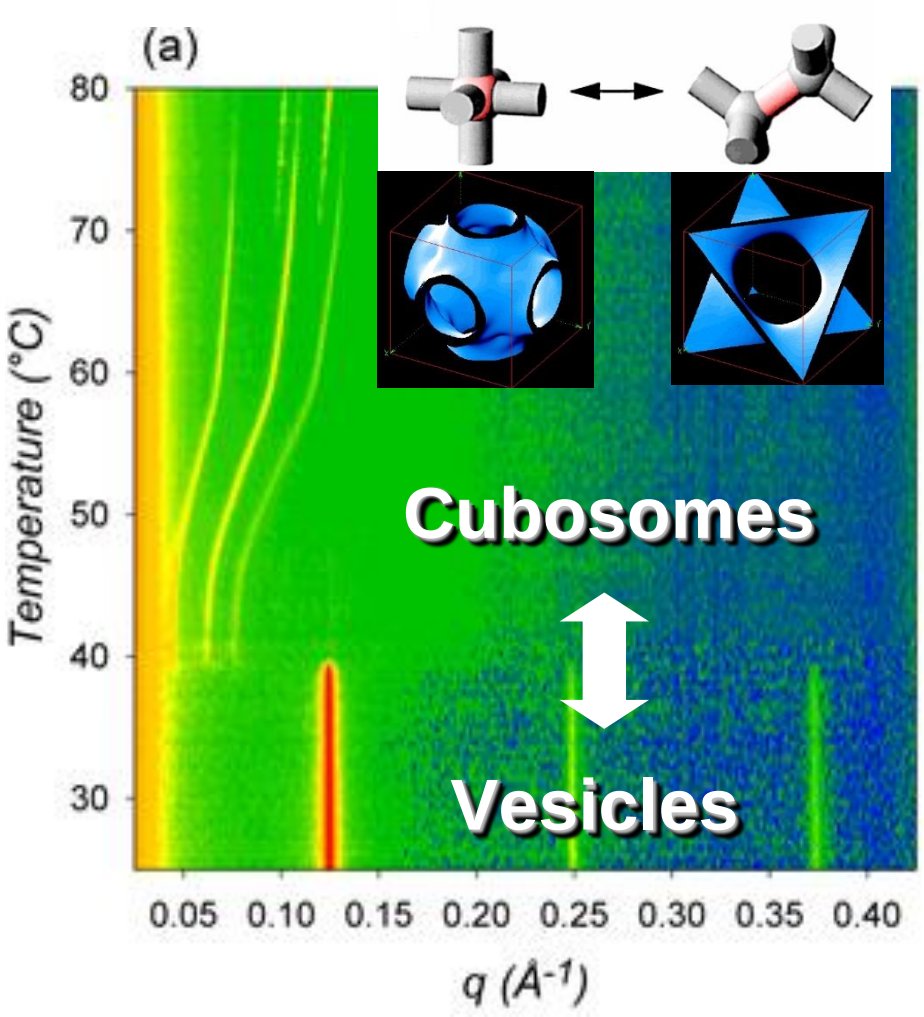
primitive phase

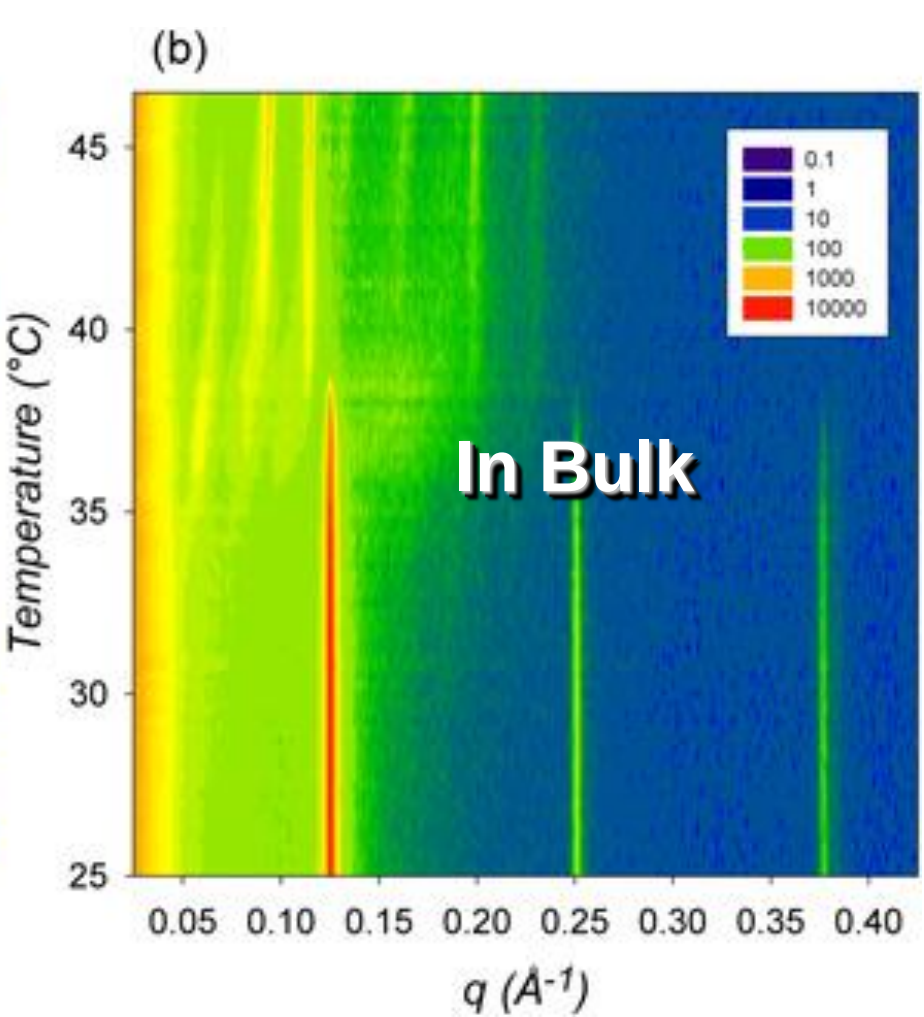
P-phase

stabilizer: e.g., pluronic

M. Rappolt In: *Advances in Planar Lipid Bilayers and Liposomes* (Vol. 5). A. Leitmannova-Liu (ed.), Elsevier Inc., Amsterdam, pp. 253-283, **2006**

# Direct Vesicle to Cubosome Transition

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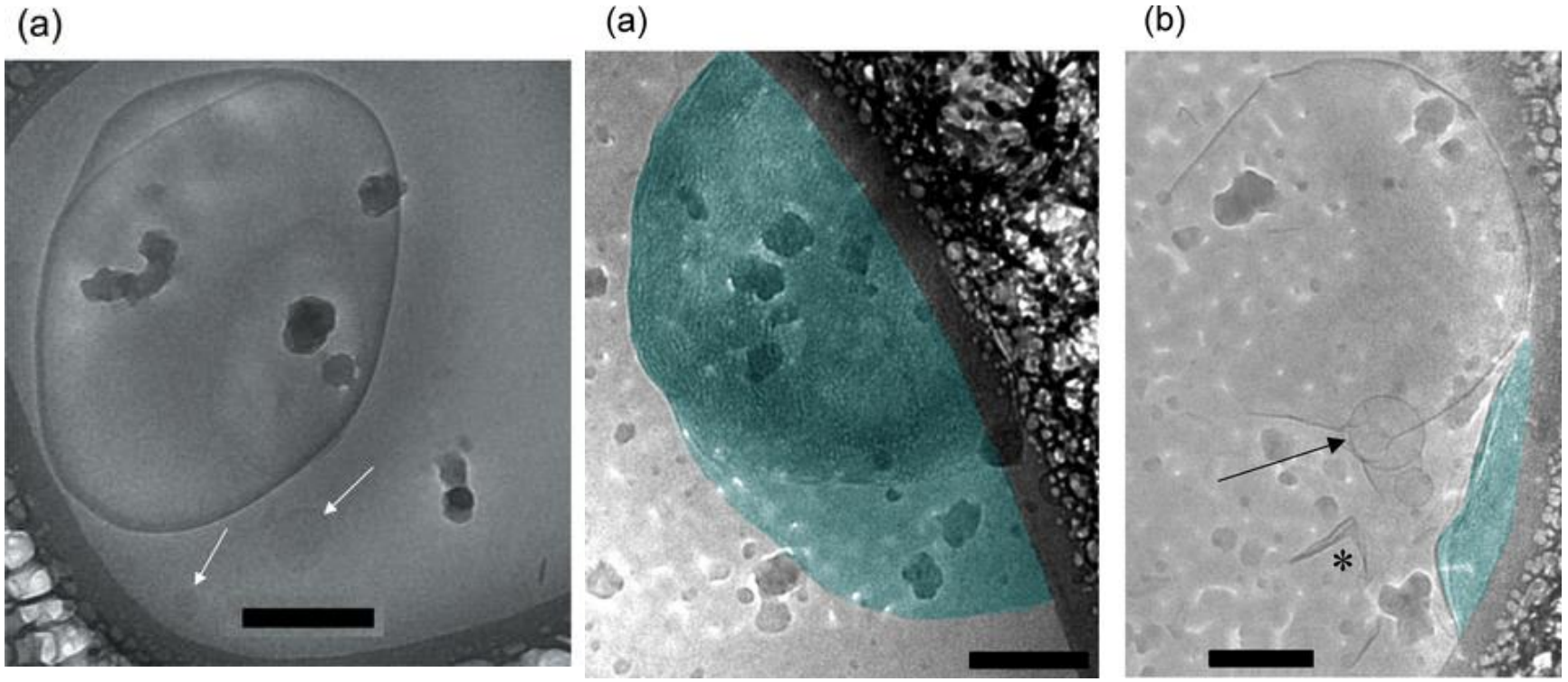
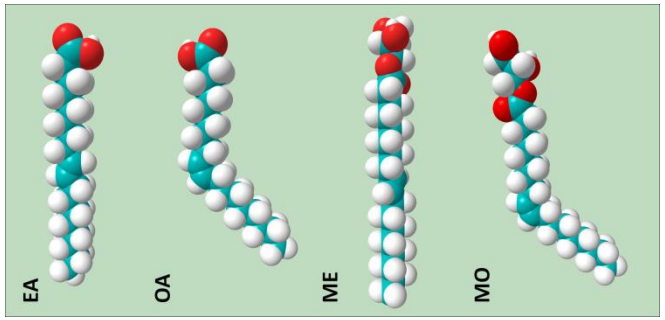
# Direct Vesicle to Cubosome Transition (II)



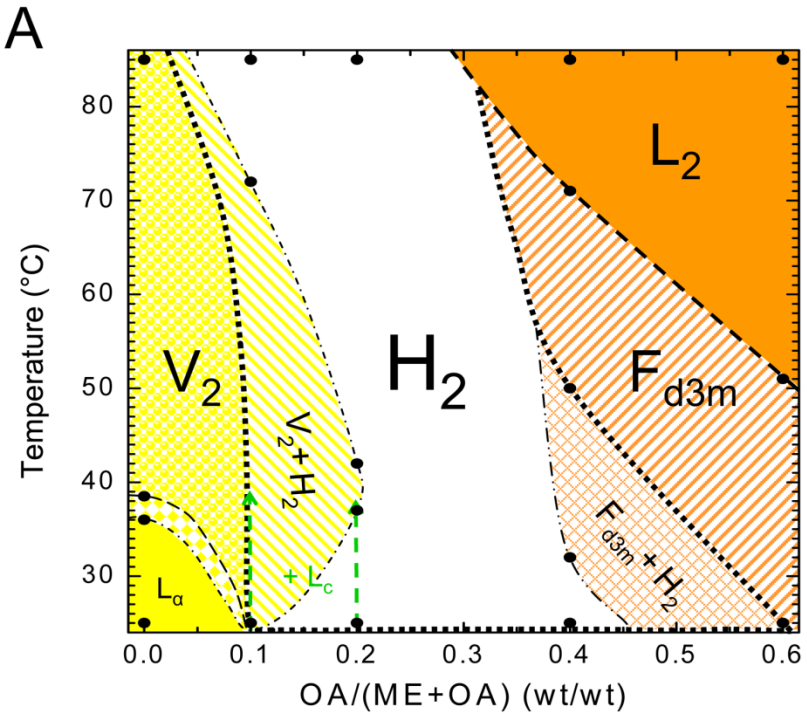

scale bar 200 nm

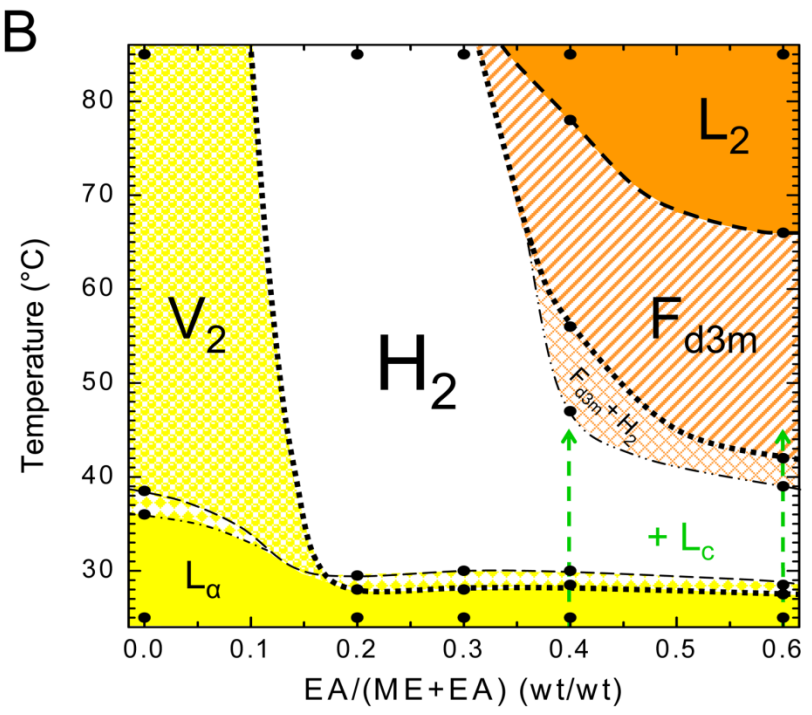
Yaghmur A, Laggner P, Almgren M, Rappolt M:
Self-Assembly in Monoelaidin Aqueous Dispersions: Direct Vesicles to Cubosomes Transition.
*PLoS ONE* 3(11): e3747 **2008**

# The Role *Trans*-Fatty Acids




Yaghmur, A., Sartori, B., and Rappolt, M. (2012): Self-Assembled Nanostructures of Fully Hydrated Monoelaidin-Elaidic Acid and Monoelaidin-Oleic Acid Systems. Langmuir 28: 10105-10119.

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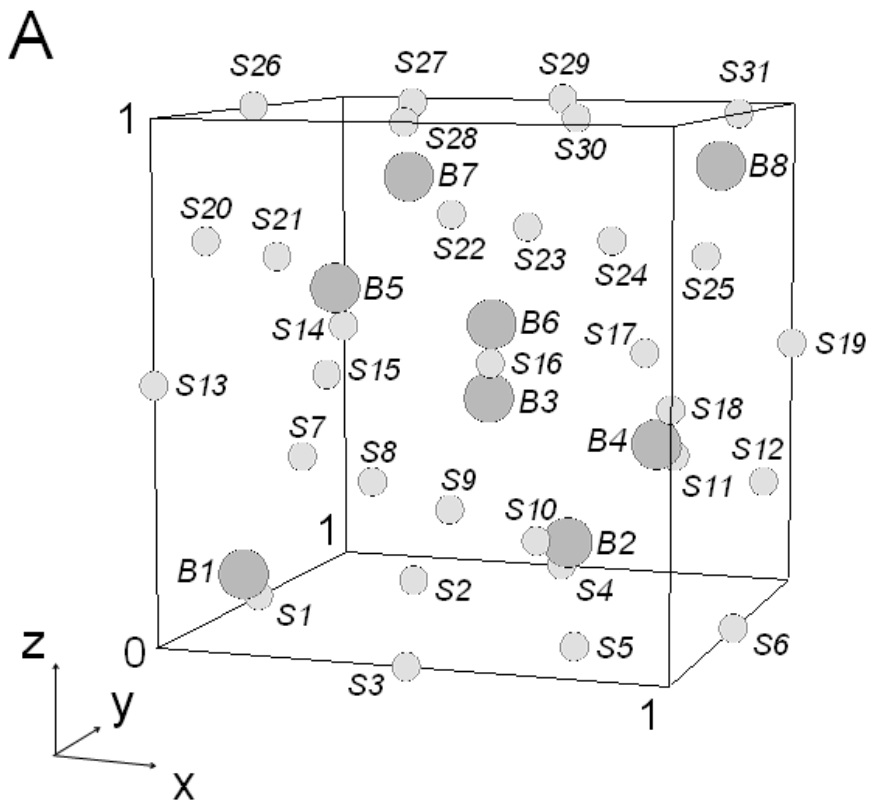
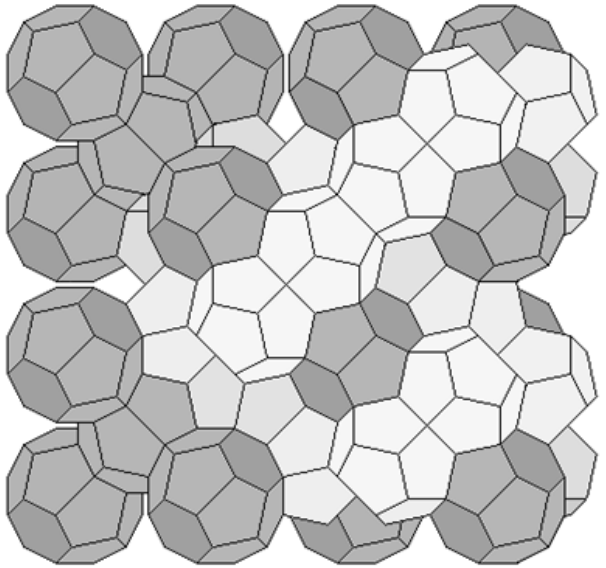
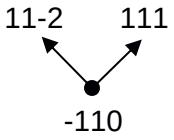
# $F_{d3m}$ Phase: Packing of „Oranges“ and „Mandarines

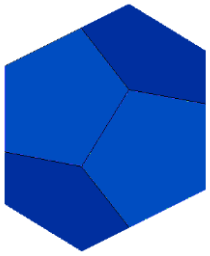


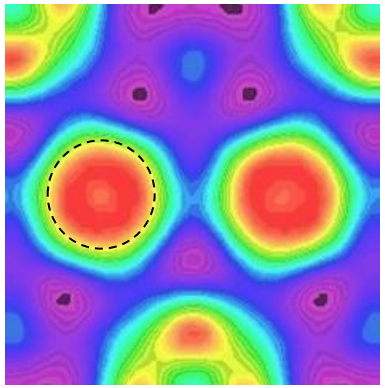

Water in oil in water emulsions are possible!

# The „Manderines“ Deform with the Addition of EA

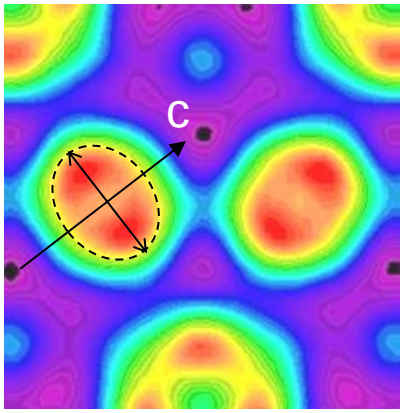


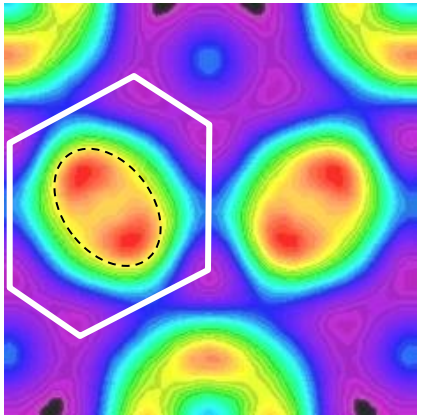
MO/OA (1:4)



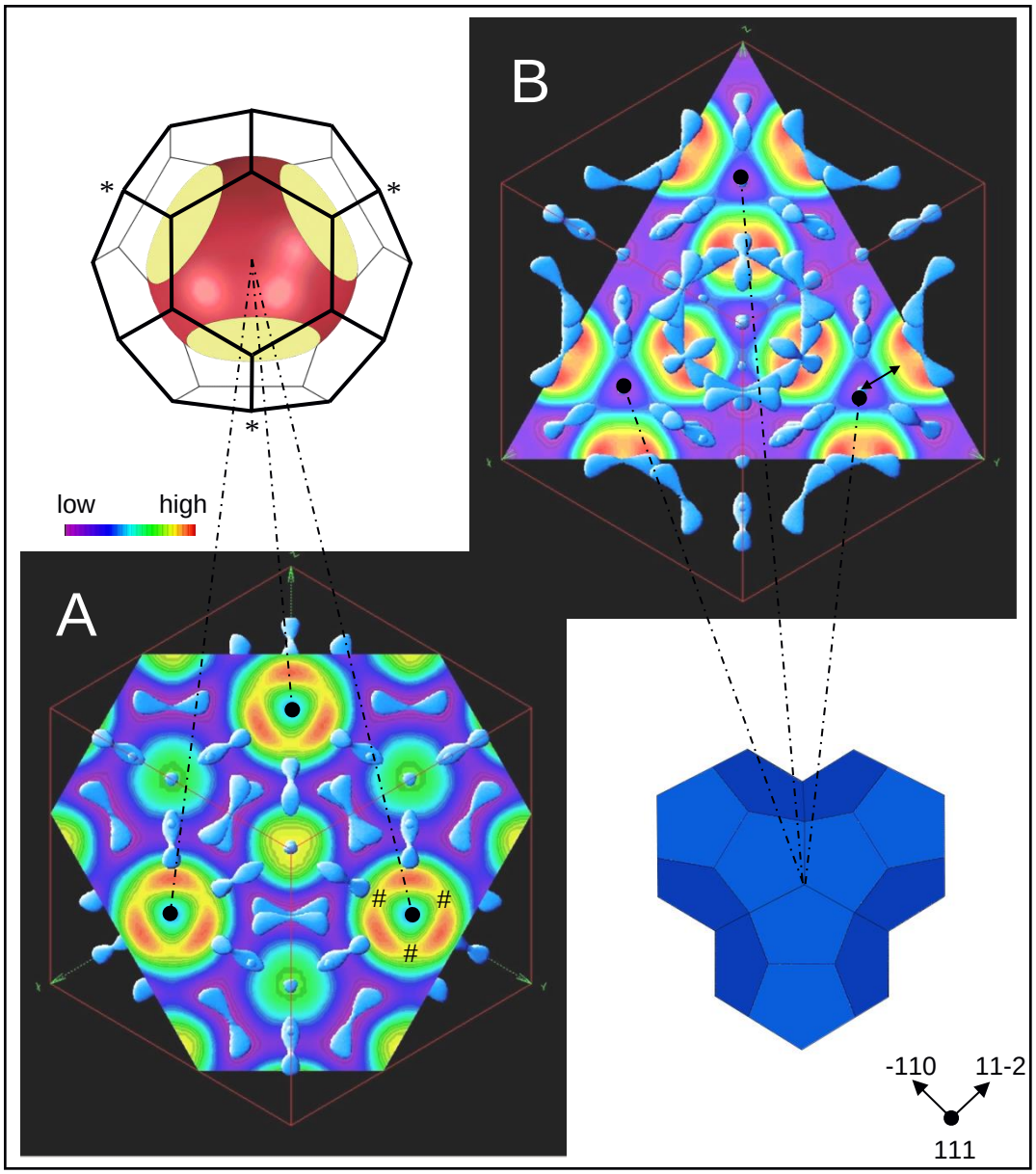
ME/OA (2:3)




ME/EA (1:1)



# The Structure of the Big Micelles

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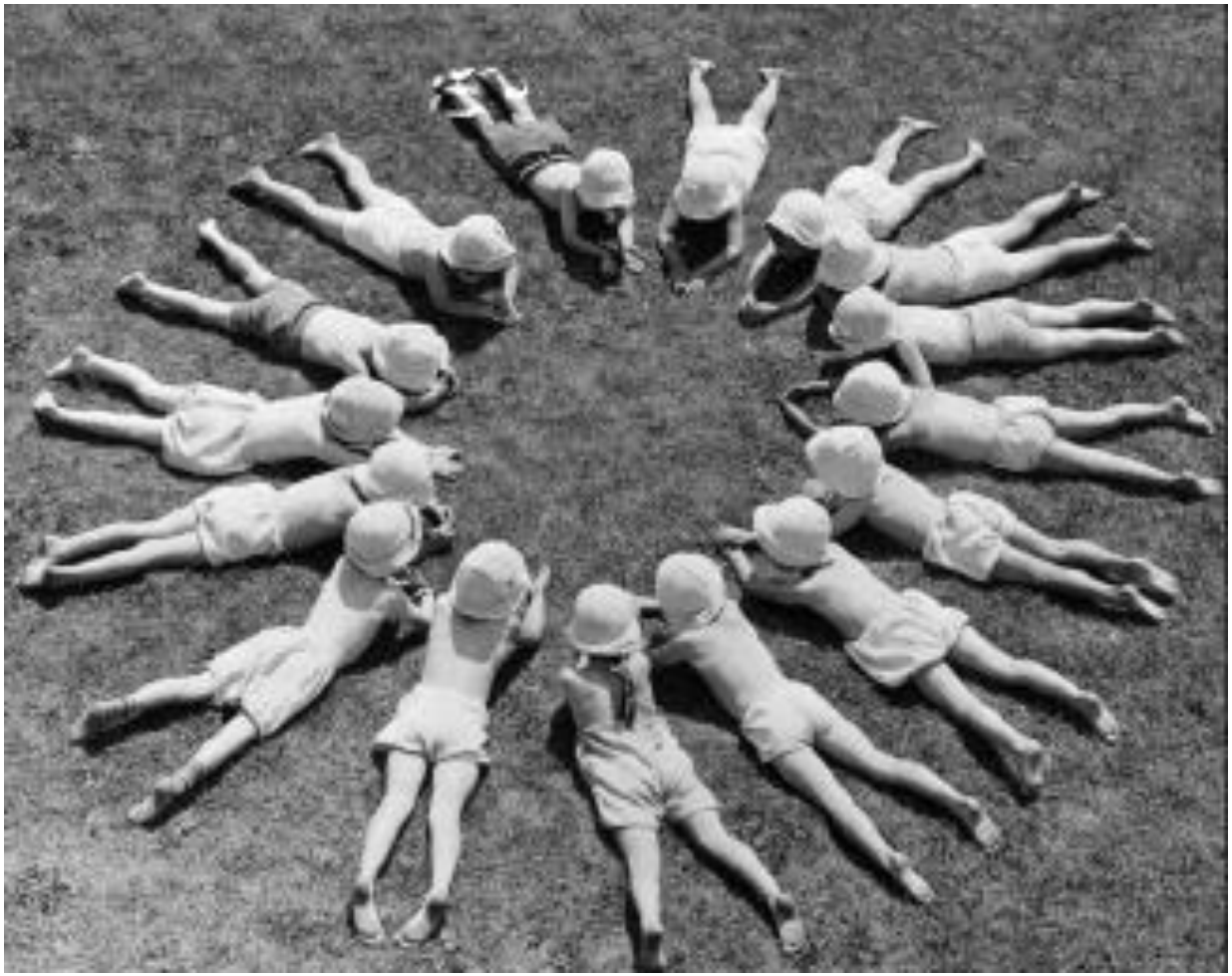
# Thank You For Your Attention!



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