Coherent diffraction imaging of single macromolecules at atomic resolution
- challenges for theory -

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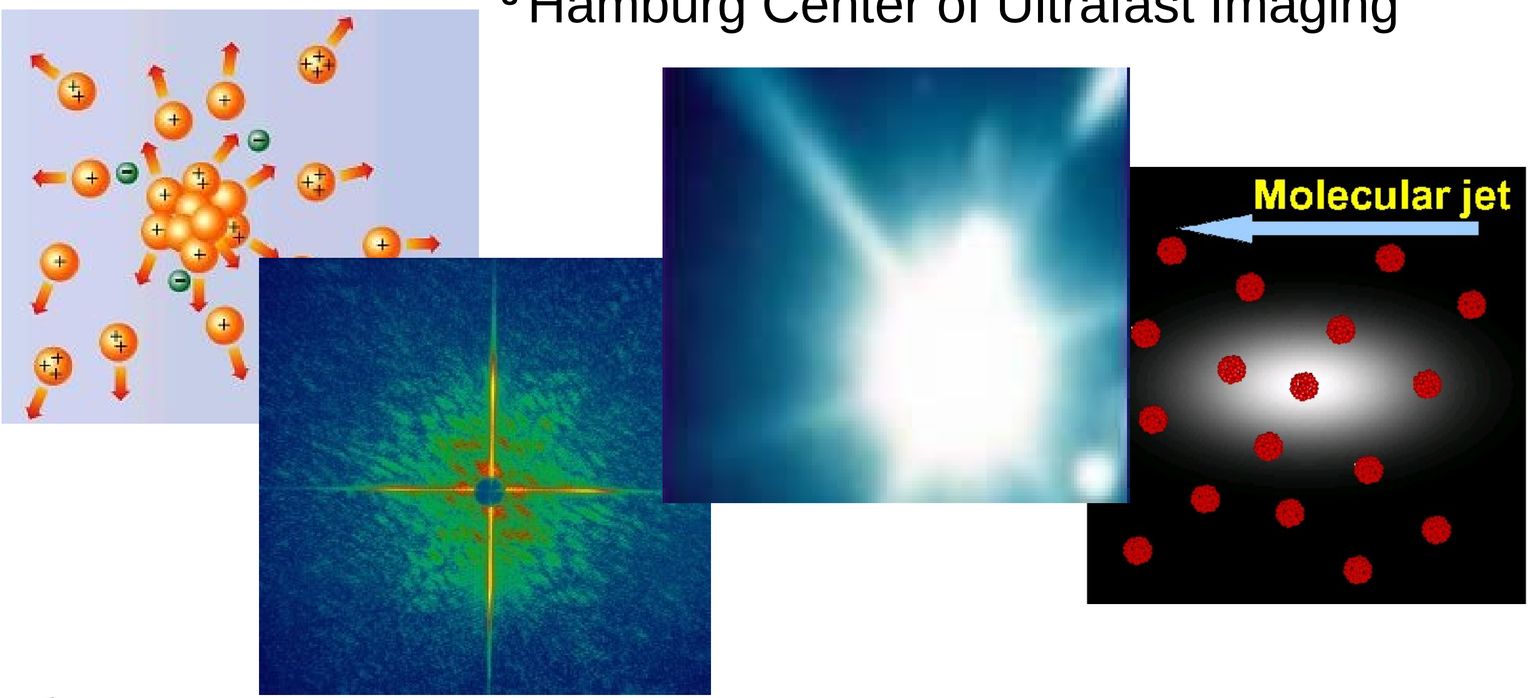
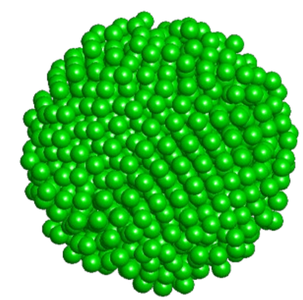
[3] Hamburg Center of Ultrafast Imaging





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CFEL-DESY Theory Division at Center for Free-Electron Laser Science

The CFEL Theory Division develops theoretical and computational tools to predict the behavior of matter exposed to intense electromagnetic radiation. We employ quantum-mechanical and classical techniques to study ultrafast processes that take place on time scales ranging from 10^{-12} s to 10^{-18} s. Our research interests include the dynamics of excited many-electron systems; the motion of atoms during chemical reactions; and x-ray radiation damage in matter.

Members of the CFEL-DESY Theory Division: C. Arnold, S. Bazzi, Y.-J. Chen, O. Geffert, D. Gorelova, L. Inhester, Z. Jurek, K. Hanasaki, A. Hanna, A. Karamatskou, M. Krishna, Z. Li, M. A. Malik, N. Medvedev, P. K. Mishra, R. Santra (Division Director), V. Saxena, J. M. Slowik, S.-K. Son, V. Tkachenko, K. Toyota, O. Vendrell, B. Ziaja

3 subgroups: 'Ab-initio X-ray Physics' (R. Santra), 'Chemical Dynamics' (O. Vendrell), 'Modeling of Complex Systems' (B. Ziaja)

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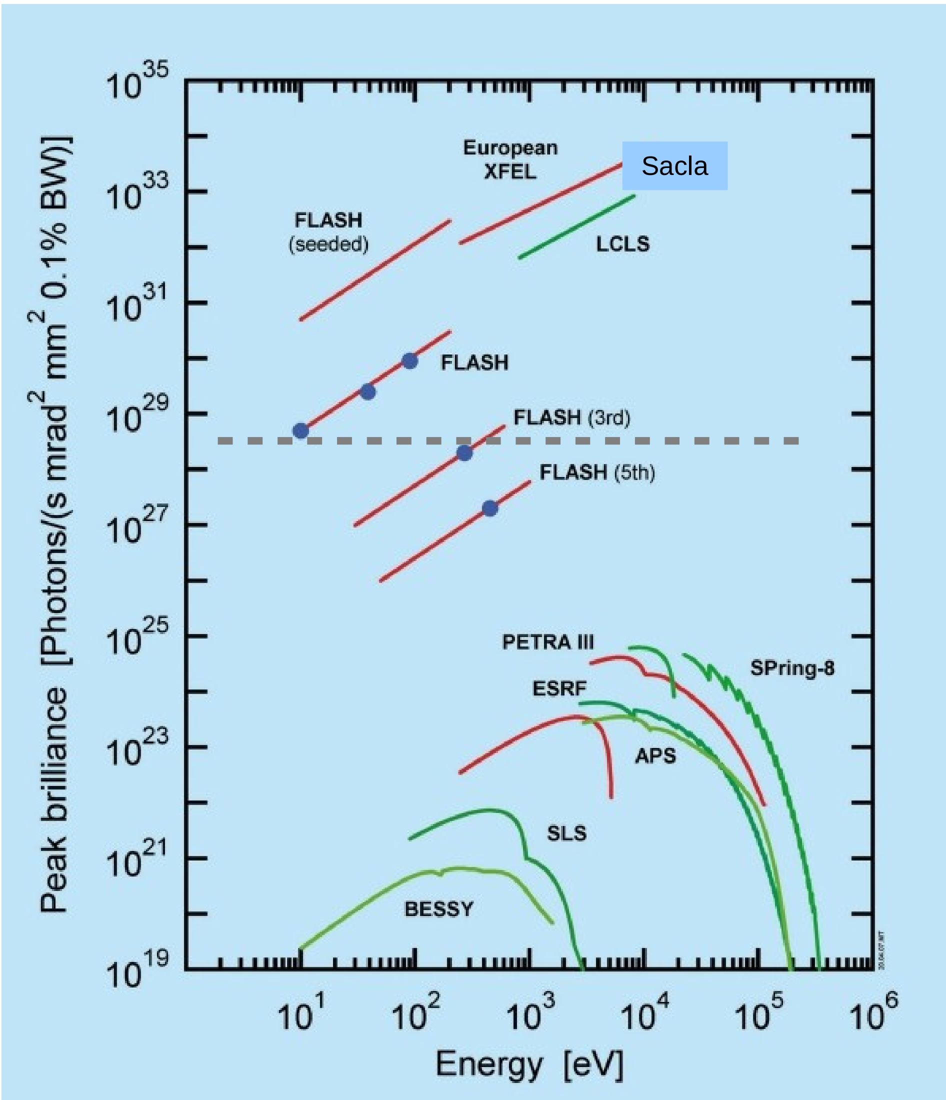
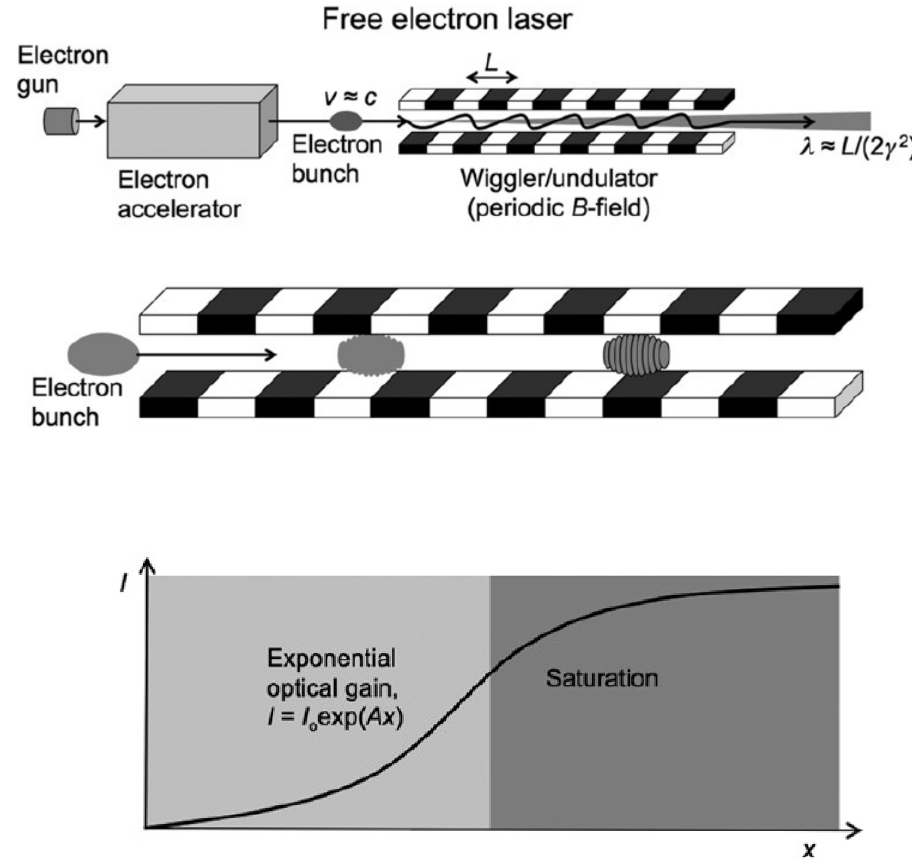
FELs: 4th generation light sources



photon-science.desy.de



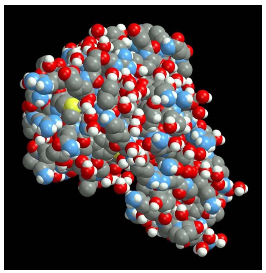
Ribic, Margaritondo, J. Phys. D **45** 213001 (2012)

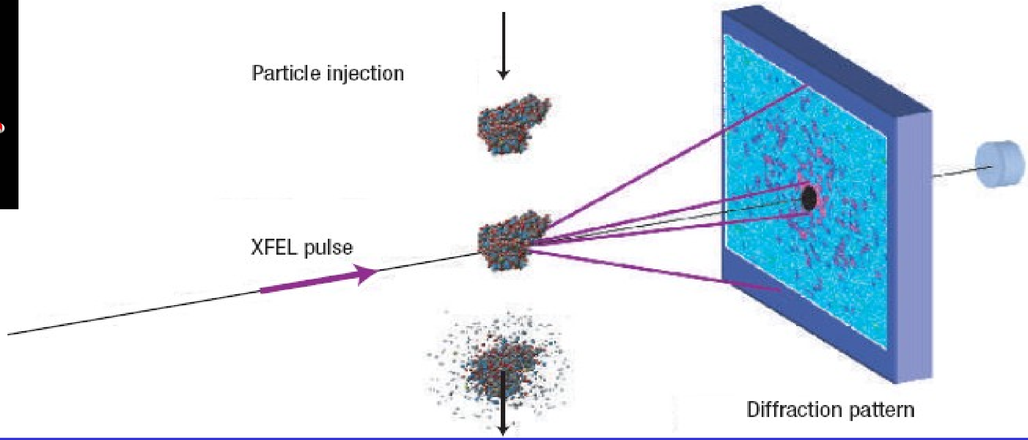
Pulse duration ~ down to 10 fs
Wavelength ~ VUV- hard X-ray

[This slide courtesy of Z. Jurek]

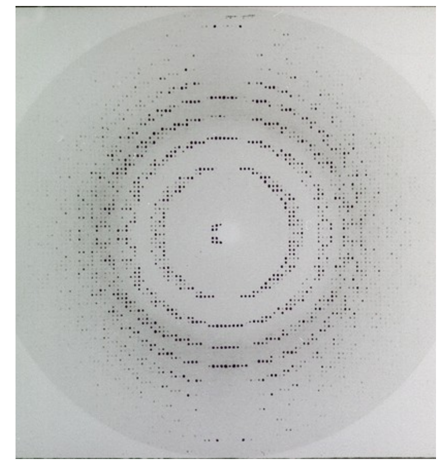
Structure determination through single particle diffraction imaging?

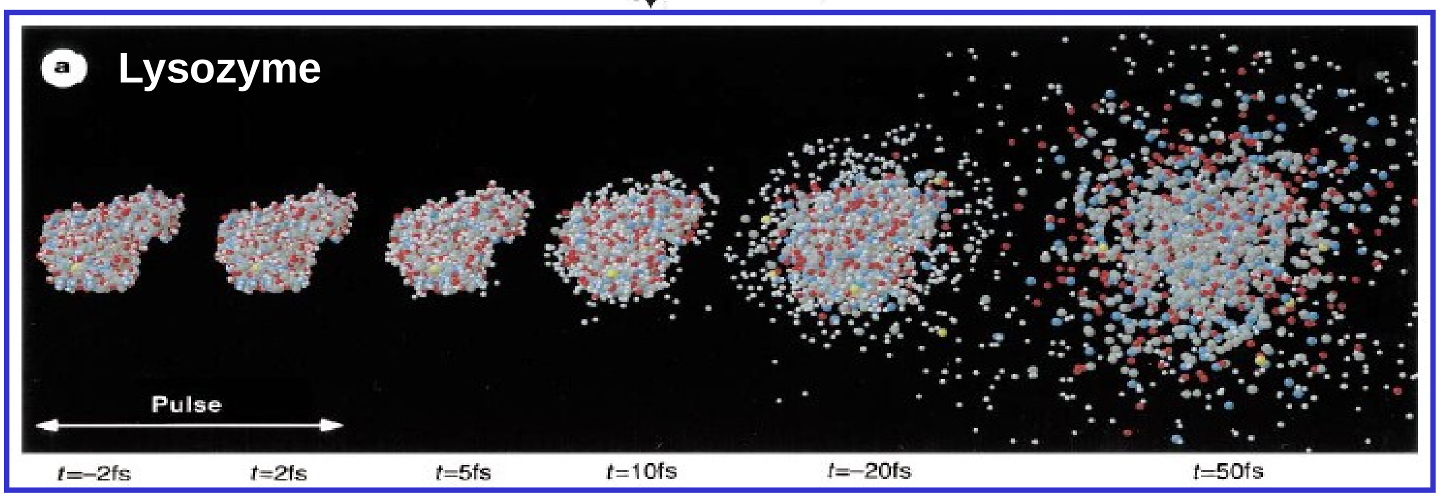
Molecules at atomic resolution





Crystal



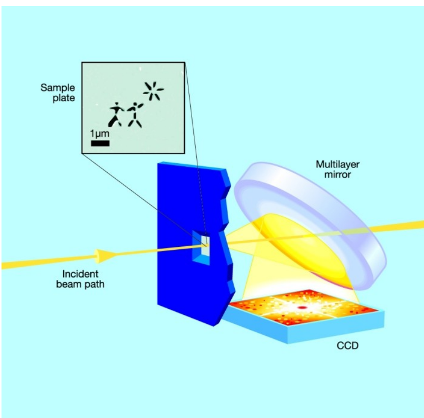


R. Neutze, R. Wouts, D. van der Spoel, E. Weckert, J. Hajdu Nature 406, 752 (2000)

Radiation damage and Coulomb explosion

Towards coherent diffraction imaging at atomic resolution ...

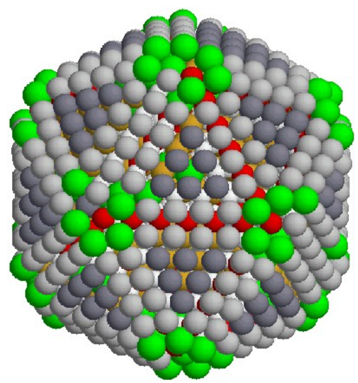
Proof of principle



[H.N. Chapman et al.,Nature Physics 2, 839-843 (2006)]

→

Cluster imaging

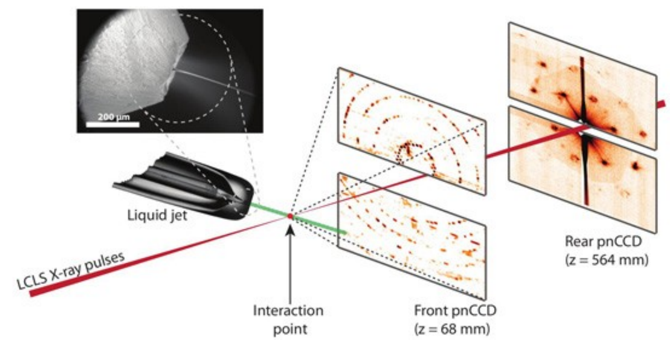


atomic cluster
© phys.canterbury.ac.nz

[T. Moeller et al., e.g., Phys. Rev. Lett. 108, 093401 (2012)]

→

Serial femtosecond crystallography



[E.g., K. Nass et al. (H.N.Chapman, I. Schlichting) J. Synchr. Rad.22, 225 (2015)]

Intense experimental effort → Impressive progress ...

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Towards coherent diffraction imaging at atomic resolution ...

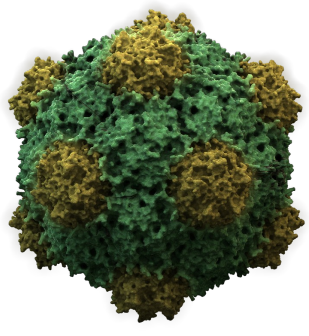
How about

hard X-ray coherent diffraction imaging

of large non-periodic reproducible samples

which structure cannot be investigated

with other experimental techniques ?



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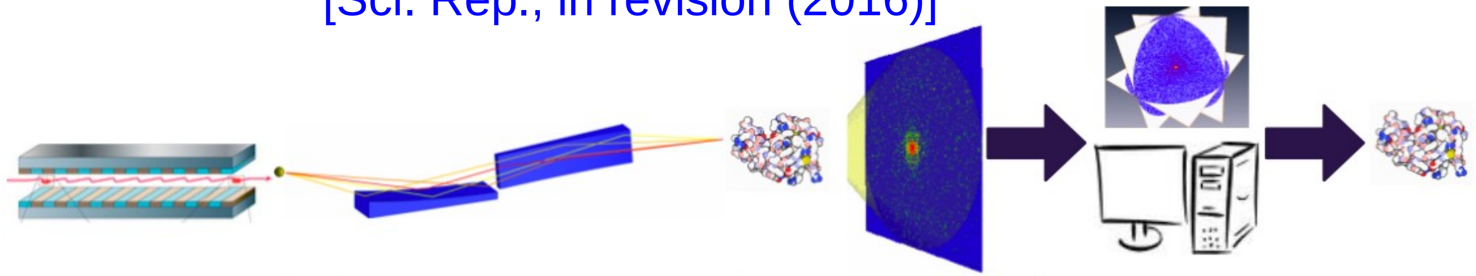
Towards coherent diffraction imaging at atomic resolution ...

Reliable theory simulations needed
to find the relevant parameter range
for X-ray pulses!

↓

Realistic simulation of an XFEL irradiated large macromolecules,
including propagation effects

linked to EXFEL beamline simulation S2E by A. Mancuso et al. (Z. Jurek. R. Santra, B. Z.)
[Sci. Rep., in revision (2016)]



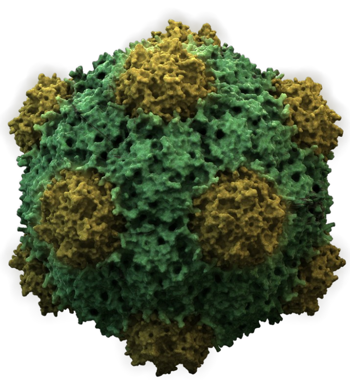
Images: *Nature Photonics* **4**, 814–821 (2010), x-ray-optics.de, pdb.org, J. Phys. B: At. Mol. Opt. Phys. 43 (2010) 194016, SPB CDR

Main interactions:

X-ray photons: elastic scattering, Compton scattering, photoionization (outer- and inner-shell), Auger decays

Electrons: collisional ionization and recombination, charge screening

Ions: electrostatic repulsion → sample expansion



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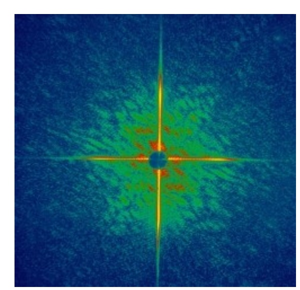
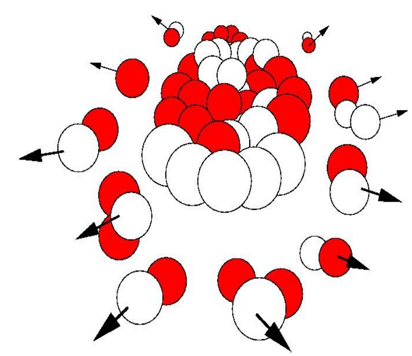
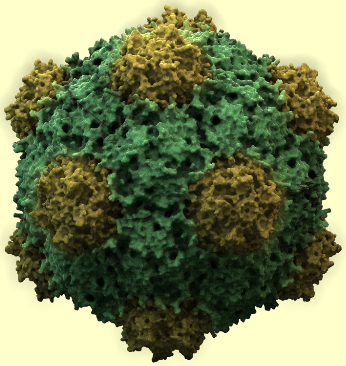
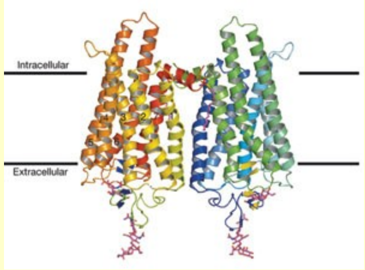




Unsolved issues and challenges in theory:

1) Contribution of inelastic scattering background to signal
2) Realistic particle size
3) Effect of interparticle correlations
4) Pulse duration (<10 fs)
5) Strongly non-equilibrium electron distribution
6) Chemical environment and plasma screening
7) Effect of spatially inhomogeneous pulse profile
8) ...





Recently solved crystal structure of the GPCR opsin

(Nature 454, 183–187; 2008).

Contribution of inelastic scattering background to signal S_{total}

$S_{total}(q,t) = S_{elastic}(q,t) + S_{inelastic}(q,t)$

$S_{elast}(q,t) = |F(q,t)|^2$

F(q,t) - Fourier transform of electronic density

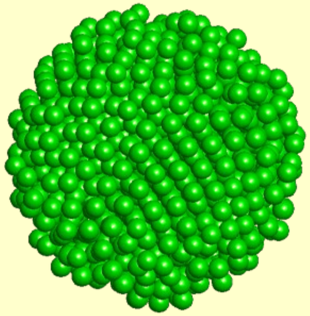
Inelastic scattering:

- for nanocrystals strong coherent Bragg peaks dominate S_{total}
- negligible at low resolution experiments on single objects
- have to be considered if planning atomic-resolution imaging of single objects.

Example: carbon cluster, 12 keV photons, fluence 10^{11}-10^{13} ph/pulse, 100 nm focus, desired resolution 1.5 Å

→ 40%-50% inelastic contribution to total signal S_{total} !

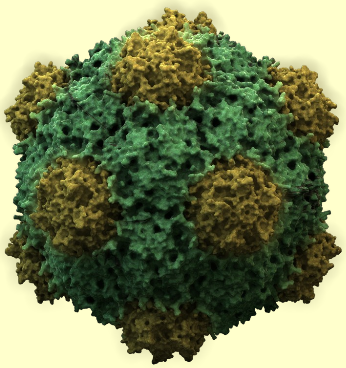
Realistic particle size



Particle large enough:

- to obtain signal-to-noise ratio appropriate for reconstruction method applied (e.g. with conventional two-step method: ~0.1 ph/speckle at a desired resolution)

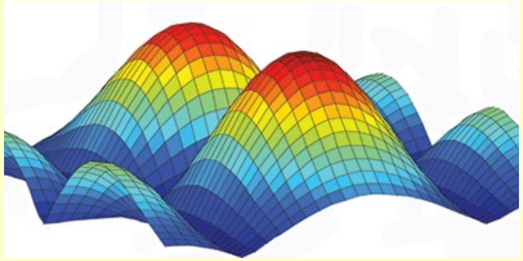
- which structure cannot be investigated with other techniques



Effect of interparticle correlations & simulation method applied

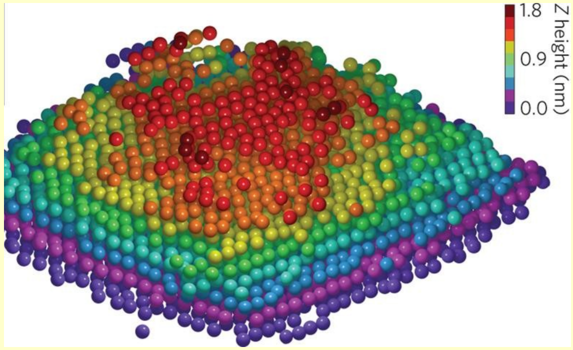
Continuum approach - based on average single-particle densities; intrinsically no two-particle correlations included

vs.



[link.aps.org]

Molecular Dynamics – simulates trajectories of classical particles (atoms, ions and electrons)



[nature.com]

Effect of pulse duration (<10 fs)

Such pulse duration is comparable with some radiation-induced

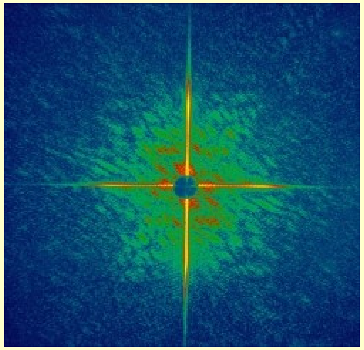
processes →

- eliminates the effects of atomic displacements

- reduction of Auger electron emission during the pulse

- reduction of damage through electrons

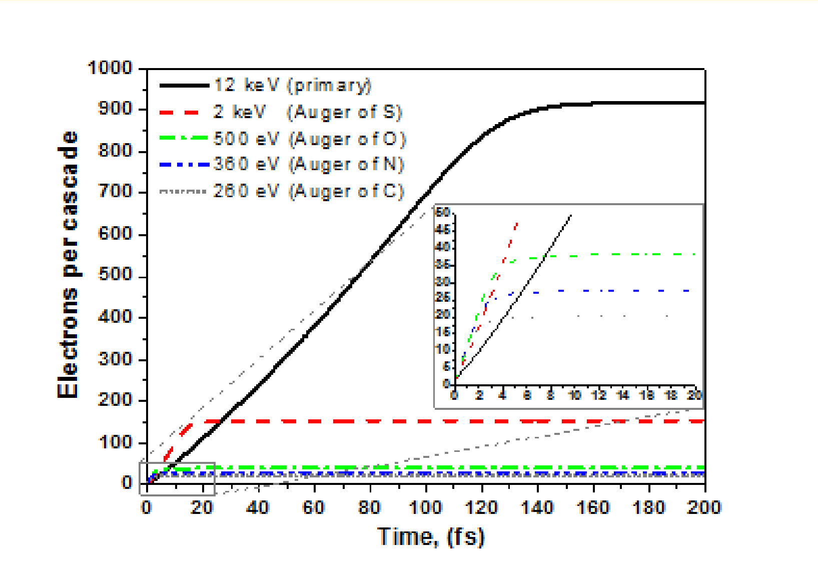
→ higher scattering power of the sample?



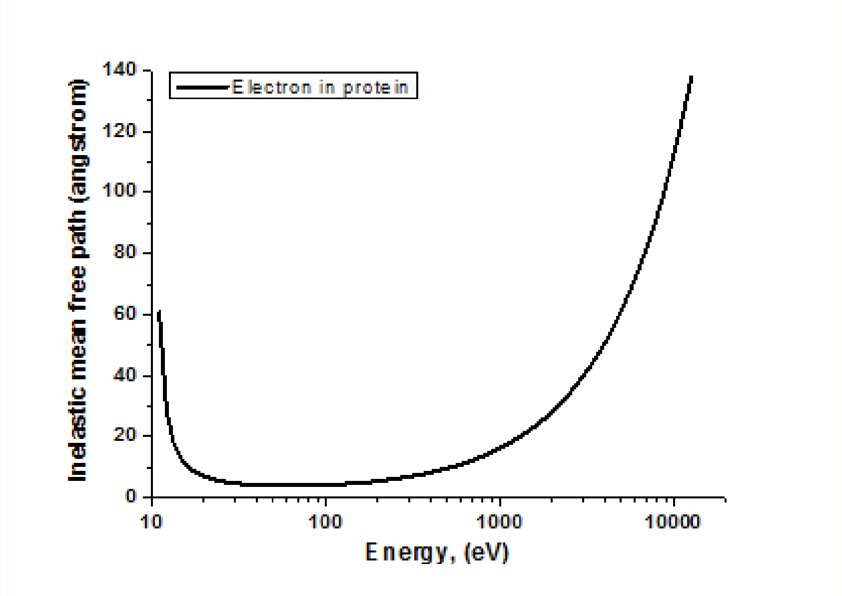
Strongly non-equilibrium electron distribution

-For short pulses (< 10 fs) photo- and Auger electrons emitted do not thermalize during the pulse → correctly represented during simulations

-Imaging with high energy photons ~ 12 keV (→ high energy photoelectrons) can reduce damage by electrons



Average number of secondary electrons created during impact ionizations by a single electron within an infinitely extended, neutral protein as a function of time.



Effective electron mean free path calculated for neutral bulk protein of density 1.35 g/cm^3 consisting of H (50 %) , C (30 %), O (10 %), N (9 %) and S atoms (1 %).

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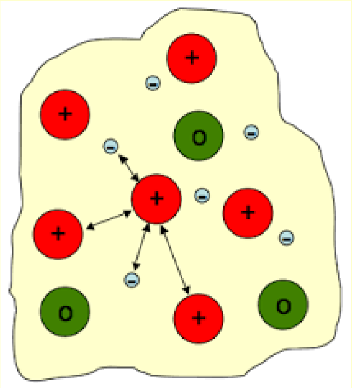
Chemical environment and plasma screening

- chemical environment can survive a lower fluence shot and influence diffraction signal
- crude approximations are used to describe chemical bonds and their breaking in molecular dynamics
- effect of charge screening by free electrons:
  - theory estimations show that atomic level shifts may be neglected with a good accuracy for few fs-long pulses
  - can plasma environment affect x-ray absorption and x-ray scattering?



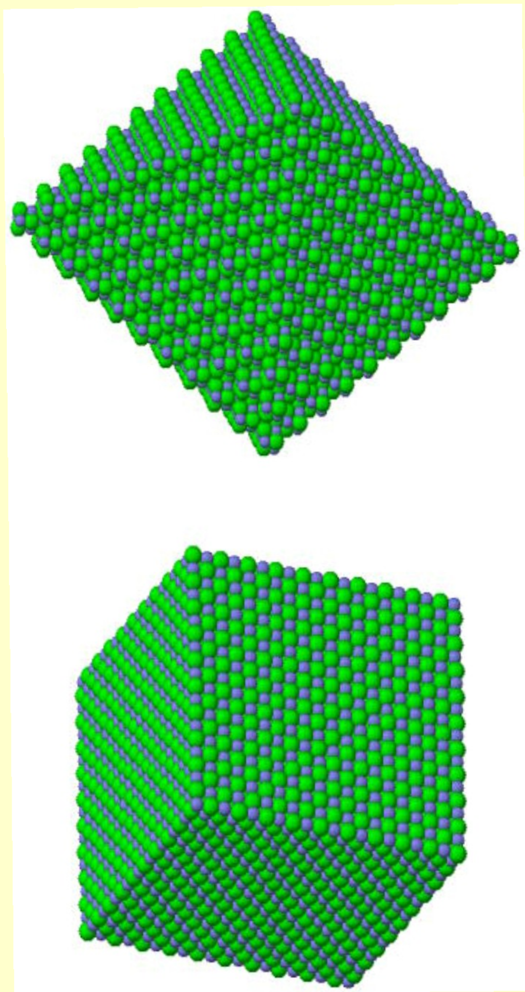
[mpnl.seas.gwu.edu]

Effect of spatially inhomogeneous pulse profile

µm large crystal ...

focus

1 µm ↕

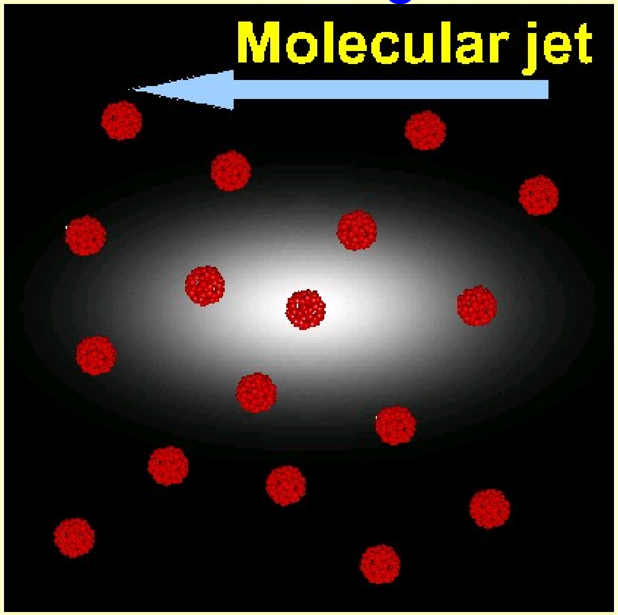


[minerva.mlib.cnr.it]

... vs 100 nm beam

few nm large cluster ...

100 nm ↕



[Courtesy of Z. Jurek]

Our in-house MD tool: XMDYN

Zoltan Jurek

- **Atomic processes** (inner- and outershell photoeffect, Auger/fluorescence decay): MC

  Rates by **XATOM** package (Sang-Kil Son, Robin Santra)

S.-K. Son & R. Santra

- **Real space dynamics**: MD
  - atoms/ions and (quasi-) free electrons: classical particles
  - classical force fields: Coulomb ; Newton's equations
- **Molecular environment** effects (chemical bonds, impact ionization,

  molecular Auger effect)
- **On-the-fly** connection to XATOM working

[Core version : Z. Jurek et al., Eur. Phys. J. D **29**, 217 (2004)]

XMDYN has been successful in modeling recent experiments:

C60@LCLS : B. Murphy et al. Nat. Commun. 5, 4281 (2014).

C60@Synchrotron : Z. Jurek, B. Ziaja and R. Santra, J. Phys. B 47, 124036 (2014).

Ar@SACLA : T. Tachibana et al., Scientific Reports 5 : 10977 (2015).

[This slide courtesy of Z. Jurek]

Example of comparison to experiment: hard X-ray irradiated Ar clusters

- **SACLA Experiment: Kiyoshi Ueda**

  T. Tachibana, H. Fukuzawa, K. Motomura, K. Nagaya,

  S. Wada, P. Johnsson, M. Siano, S. Mondal, Y. Ito, M. Kimura,

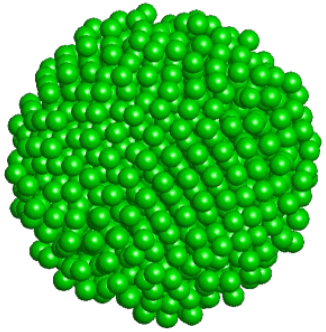
  T. Sakai, K. Matsunami, H. Hayashita, J. Kajikawa, X.-J. Liu, E. Robert,

  C. Miron, R. Feifel, J. P. Marangos, K. Tono, Y. Inubushi, M. Yabashi,

  M. Yao

- **Theory: CFEL Theory Division**

  Z. Jurek, S.-K. Son, B. Ziaja, R. Santra



Irradiation conditions:
- Eph = 5 – 5.5 keV
- T = 10 fs
- ε ~ 0.24 mJ

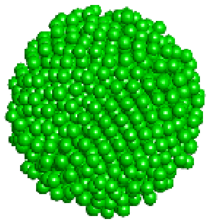
Electron data measured

[T. Tachibana *et al*, Sci. Rep. 5, 10977 (2015)]

[This slide courtesy of Z. Jurek]

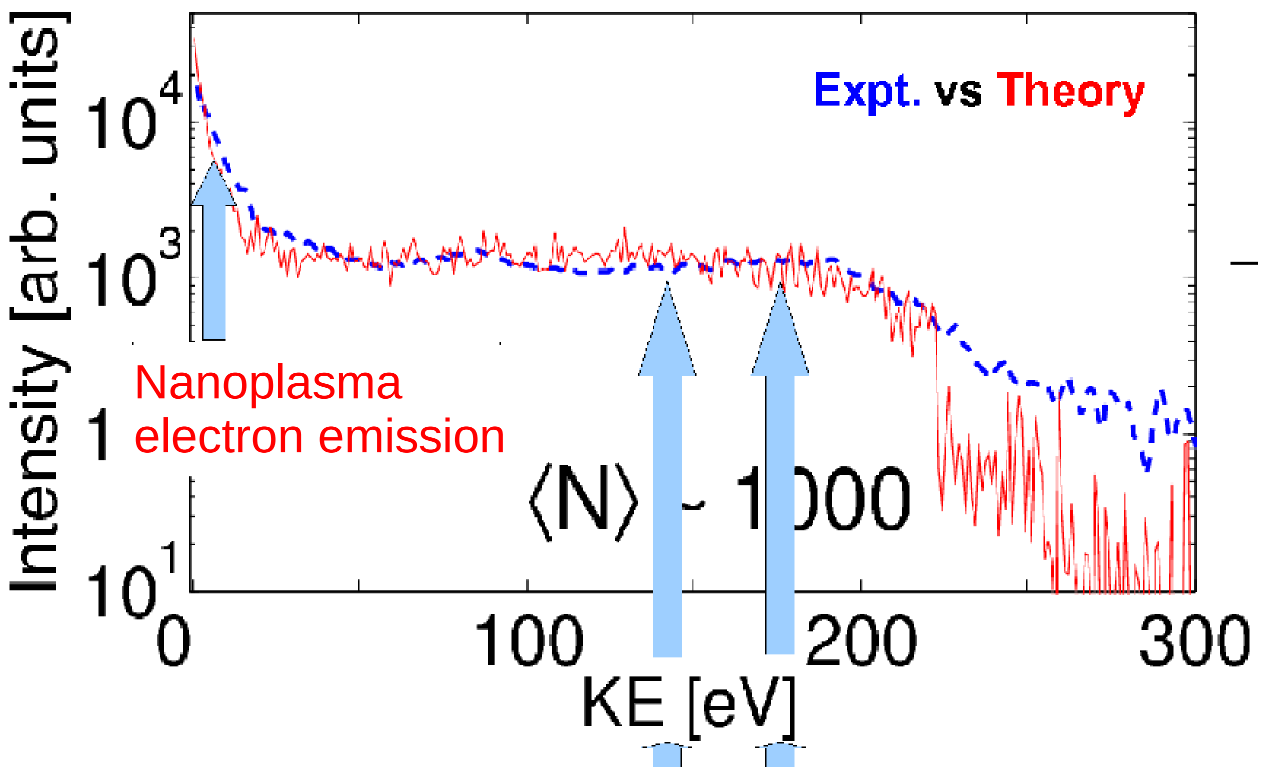
Example of comparison to experiment: hard X-ray irradiated Ar clusters

> **Theoretical and experimental electron kinetic energy spectra**,



Ar_{1000}

$\hbar\omega$ = 5keV, T=10fs



– Theory:

No parameter fitting!

Slowed-down LMM Auger electrons

T. Tachibana *et al*, Sci. Rep. accepted (2015)

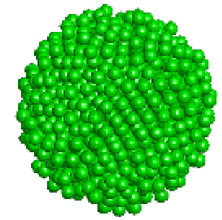
[This slide courtesy of Z. Jurek]

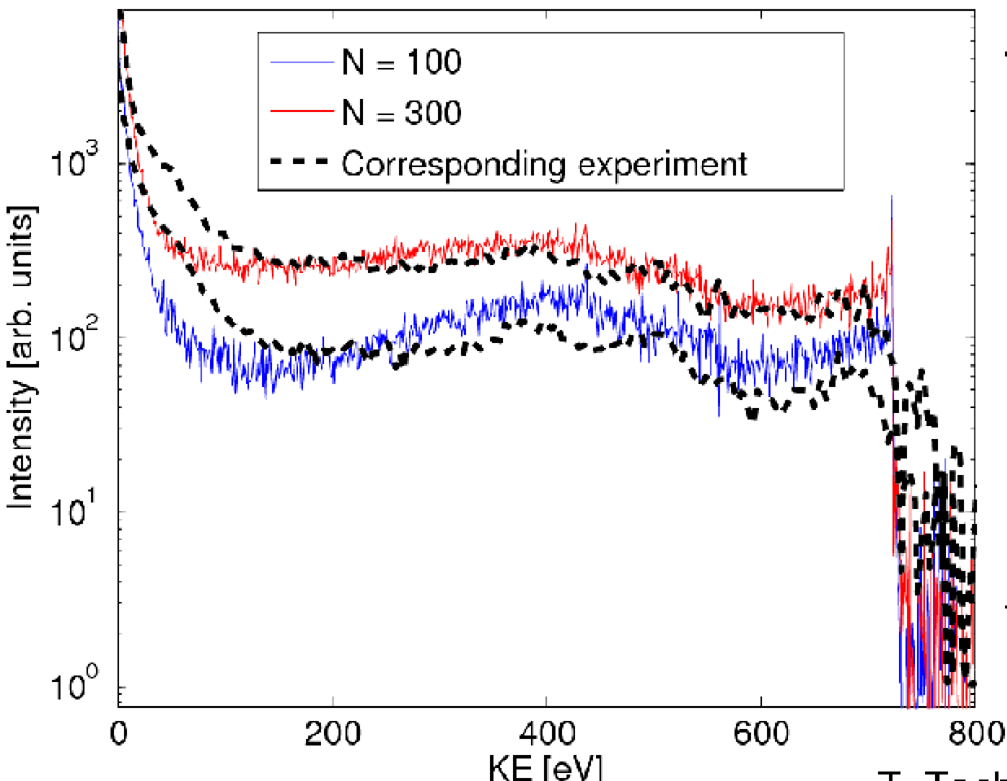
Example of comparison to experiment: hard X-ray irradiated Xe clusters

> **Theoretical and experimental electron kinetic energy spectra**,

ħω = 5.5keV, T=10fs

Xe_{100}, Xe_{300}





– Challenge for Theory:

23.532.201 possible

electronic configurations / atom!

XATOM —on-the-fly→ XMDYN

– Theory:

No parameter fitting!

T. Tachibana *et al*, Sci. Rep. accepted (2015)

[This slide courtesy of Z. Jurek]

Development of XMDYN code

- **Large-scale MD able to simulate irradiation of complex molecular systems consisting of 10^{6} particles → tree algorithm implemented**

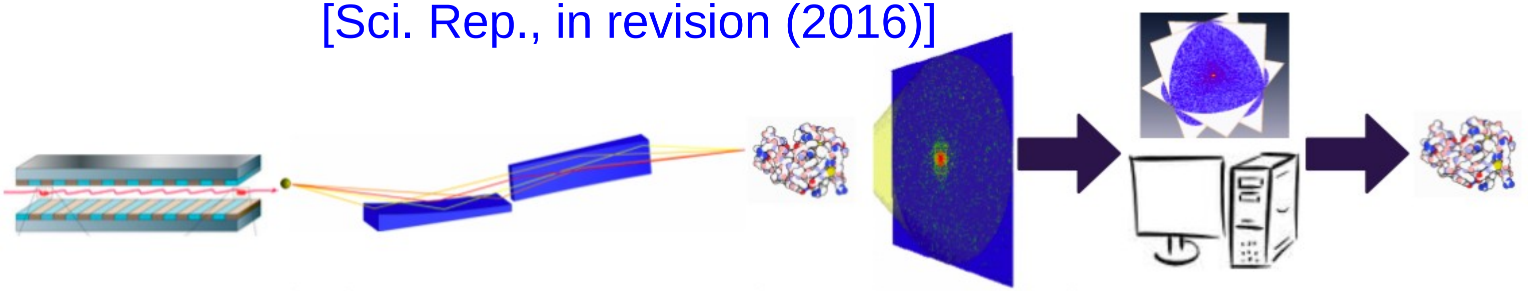
- **Coupling to the XATOM code, enabling to follow 'on-the-fly' various atomic configurations (including rate and cross section calculations) → crucial for high Z elements**

- **Large-scale simulations of macromolecules after electron thermalization with XHYDRO code → both electrons and ions are treated hydrodynamically → computationally efficient, enables stable propagation on long timescales**

↓ ↓ ↓

Application: coherent diffractive imaging (CDI) → realistic simulation of an XFEL irradiated large macromolecules, including propagation effects (linked to EXFEL beamline simulation S2E by A. Mancuso et al.)

[Sci. Rep., in revision (2016)]



Images: *Nature Photonics* **4**, 814–821 (2010), x-ray-optics.de, pdb.org, J. Phys. B: At. Mol. Opt. Phys. 43 (2010) 194016, SPB CDR

[Image courtesy of Z. Jurek]

Summary

- **Biological samples are highly radiation sensitive. The rapid progress of their radiation damage prevents accurate structure determination of single macromolecular assemblies in standard diffraction experiments.**

- **Theory simulations of the damage formation have shown that the radiation tolerance might be extended at very high intensities with ultrafast X-ray imaging**

- **In particular, theoretical simulations try to address an important question: How does the radiation damage progressing within an imaged single object limit the structural information about this object recorded in its diffraction image during a 3D imaging experiment?**

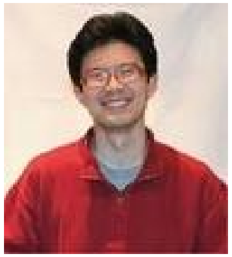
- **We discussed unsolved issues and challenges for simulations of X-ray irradiated single molecules relevant for imaging studies. They should be addressed during further development of these simulation tools.**

Thanking my collaborators ...

Z. Jurek

R. Santra

S.-K. Son



V. Saxena

N. Medvedev

"Towards realistic simulations of macromolecules irradiated under the conditions of coherent diffraction imaging with an X-ray free-electron laser“, B. Ziaja, Z. Jurek, N. Medvedev, V. Saxena, S.-K. Son, R. Santra, Photonics 2, 256-259 (2015)

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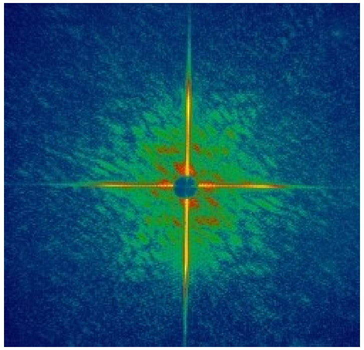
Thanking our experimental collaborators...



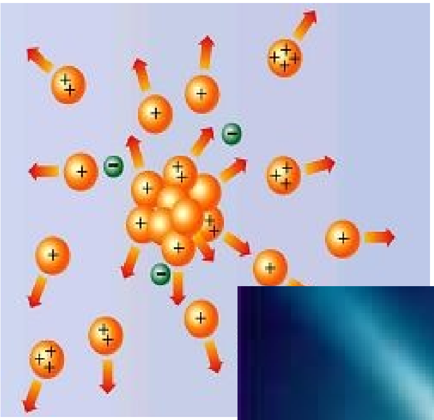
H. N. Chapman & CI Division (CFEL)

J. Hajdu, N. Timneanu, C. Caleman (Uppsala Univ.)

L. Juha, M. Stransky (FZU, Prague)

A. Mancuso & S2E Team(EXFEL)

S. Toleikis (DESY)



I. Schlichting (MPI for Medical Research)

K. Ueda & Team(SACLA)

and ...

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Thank you for your attention !