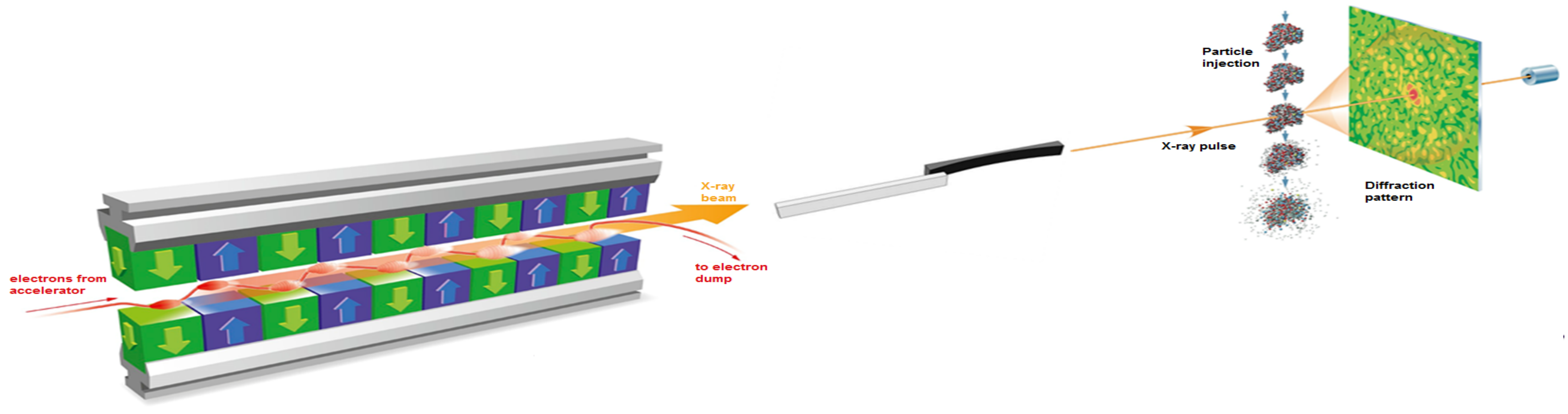
Start-to-end simulations of experiments at the European XFEL

Carsten Fortmann-Grote, Adrian P. Mancuso

Scientific Instrument SPB-SFX

July 3rd 2018

EUCALL Workshop on Theory and Simulation of Photon-Matter Interaction



European XFEL

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 654220

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Outline

- Introduction: Diffractive Imaging Experiments at the European X-ray Free Electron Laser
- The SIMEX experiment simulation platform
- Elements of s2e simulations (“Start – to – end” or “Source – to – Experiment”)
    - Photon Sources
    - Photon propagation
    - Photon – Matter Interaction and Signal Production
    - Detectors
- Applications to Imaging experiments
    - Pulse length dependence of diffraction data “interpretability”
    - Imaging of hydrated molecules
    - Imaging on inorganic particles
- Summary and Outlook

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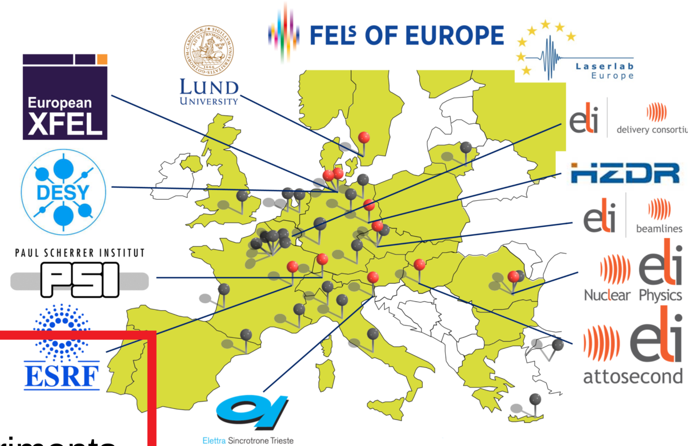
Seven EUCALL work packages address problems and research opportunities common to x-ray and optical laser community



- **WP 1 – Management of the EUCALL Project**
- **WP 2 – Dissemination and Outreach**
- **WP 3 – Synergy of Advanced Laser Light Sources**
- **WP 4 – SIMEX: Simulation of Experiments**
  - Start-to-end simulation platform for photon-science experiments
- **WP 5 – UFDAC: Ultra-fast Data Acquisition**
  - Data processing for femtosecond and attosecond pulsed photon sources
- **WP 6 – HIREP: High Repetition Rate Sample Delivery**
  - Integrated concept for decentralized sample characterization and fast sample positioning
- **WP 7 – PUCCA: Pulse Control and Characterization**
  - Pulse arrival time measurement, wavefront sensing, transparent intensity monitor

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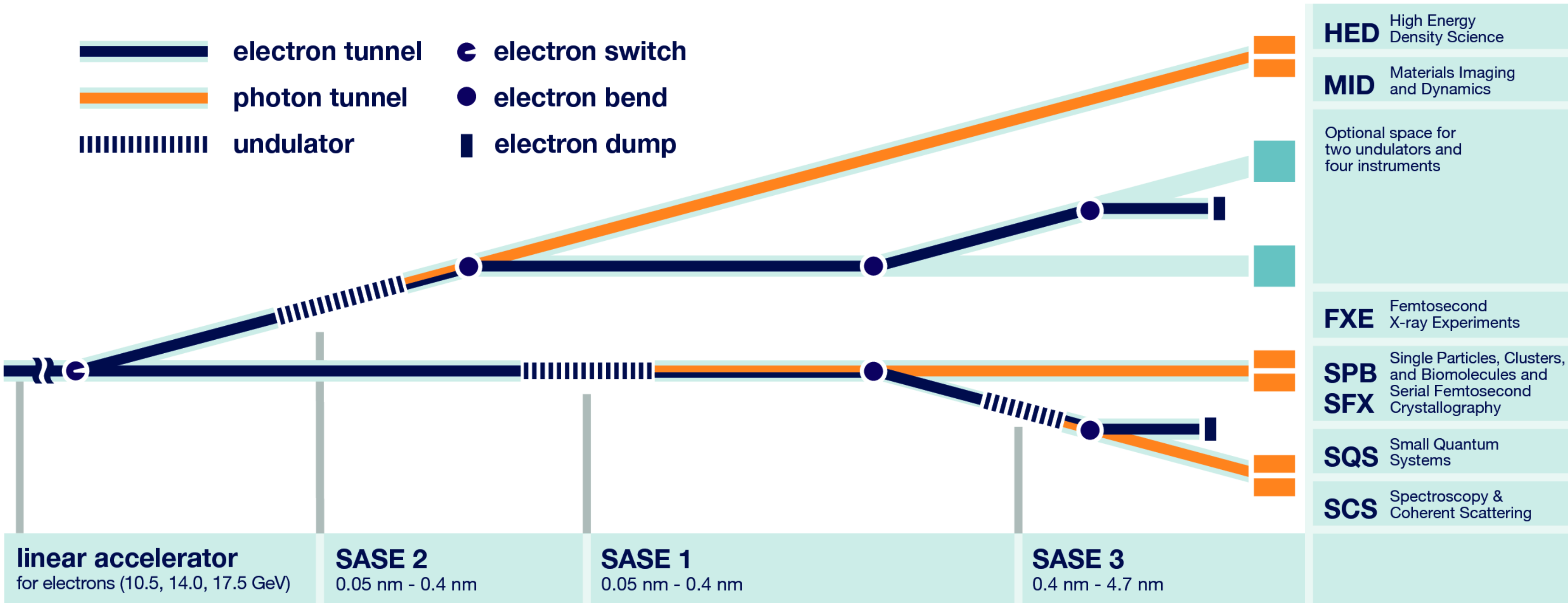
European XFEL SASE Beamlines and Scientific Instruments



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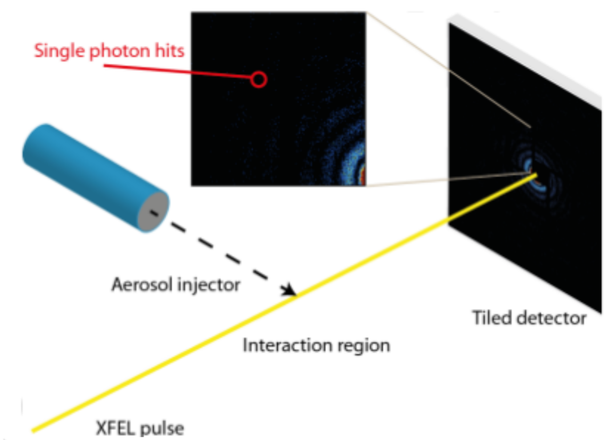
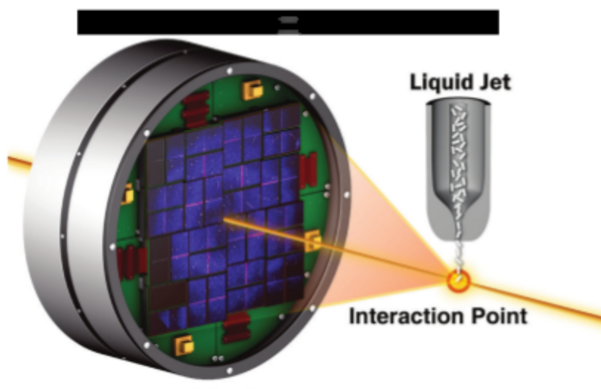
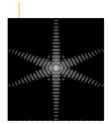
The three canonical SPB/SFX-type experiments

Weakly scattering objects
(**B**iomolecules)



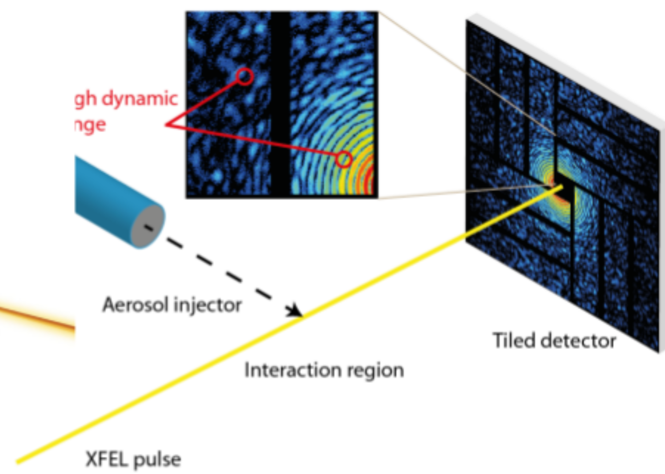
Nanocrystallography (**SFX**)





Simulated diffraction pattern around a Bragg peak produced from an icosahedral nanocrystal

“Not-so-weakly” scattering objects
(Cluster, **P**articles)



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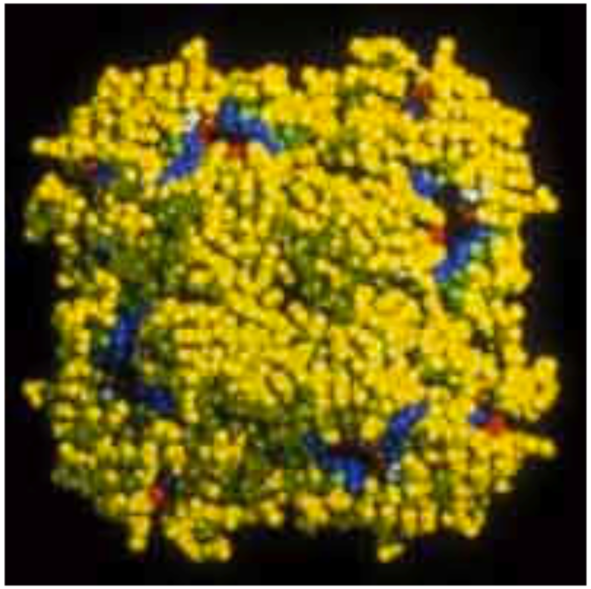
Why image biomolecules?

Why image *single* biomolecules?

- Structure of a molecule ⇒ function
- Understanding the structure allows, e.g., Rational Drug Design, Understanding of human biochemistry.
- Photons (X-rays) extract volumetric information from intact systems.
- Single Particle Imaging seeks to image molecules and structures that are *unable to be imaged by other means*. These are structures < microns in size and include membrane proteins (that don't crystallize).

Review: A. P. Mancuso, *et al*, J. Biotechnol. **149** (2010) 229–237



Influenza virus structure
- A protein from the influenza virus

Image: J.Varghese et al, CSIRO Health Science & Nutrition

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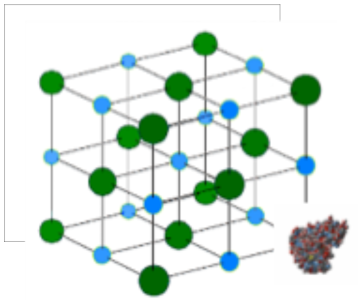
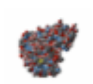
Non-crystalline material scatters fewer x-rays than crystalline material



Scattered x-rays is proportional to N^2
(~ 100 x 100 x 100 elements)



One molecules scatters like... 1
(~ a million times less than above)

- Conclusion: Need a lot more x-rays to see a single particle
- First guess solution: Just leave the x-ray tap on for longer!

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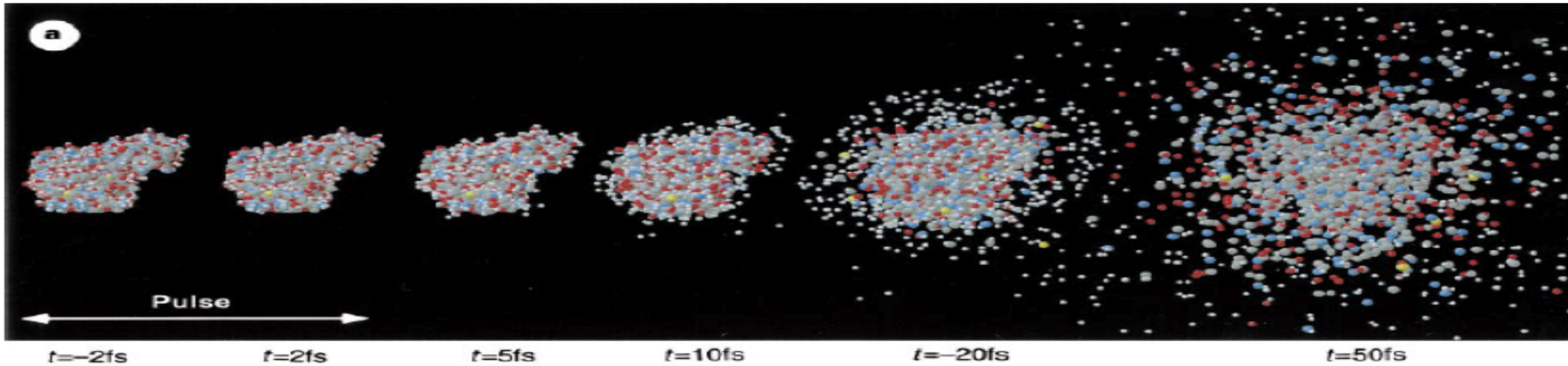
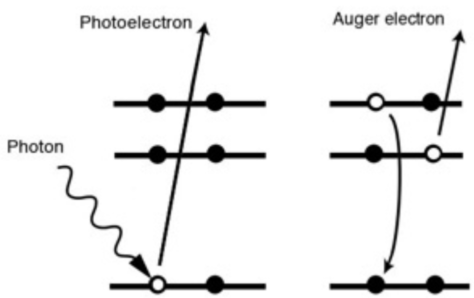
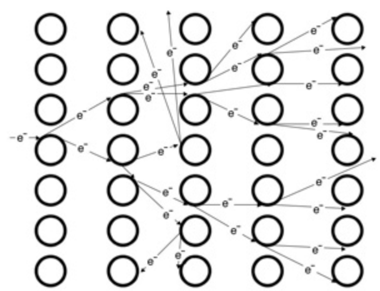
Radiation damage: A multiphysics – multiscale problem



Neutze et al. Nature (2000)





- Electronic structure
- Ionization
- Nanoplasma
- Coulomb explosion
- Hydrodynamics

Element	τ_{Auger}(fs)
C	10.7
N	7.1
O	4.9
P	2.0
S	1.3

Ultrashort pulses (few fs) may outrun secondary ionization and hydrodynamic expansion

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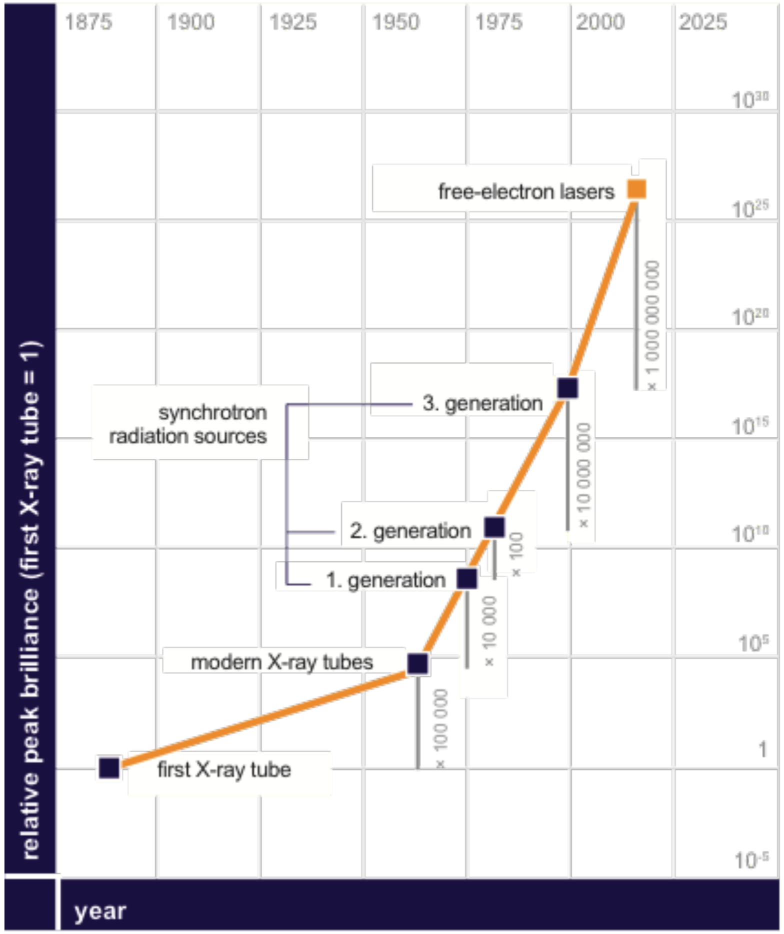
Free Electron Lasers produce intense pulses, short enough to support “diffract-before-destroy”



with pulse durations as short as femtoseconds

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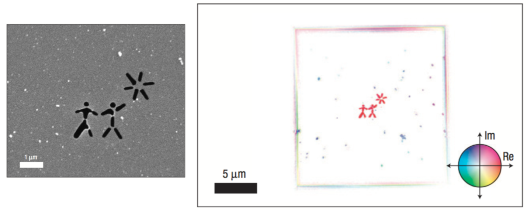
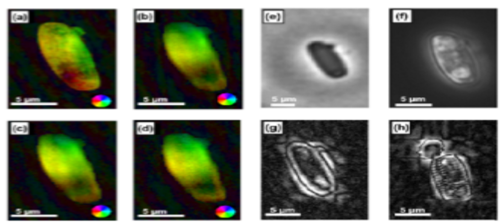
Milestone Experiments

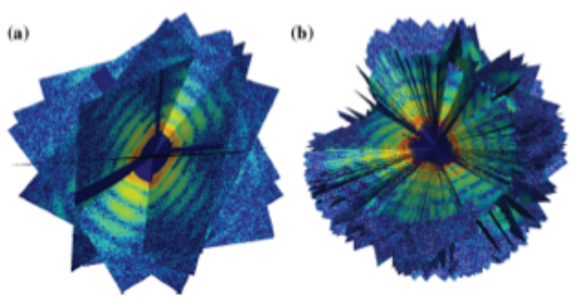
- Proof of principle: Chapman et al., Nature Physics **2**, 839 (2006)

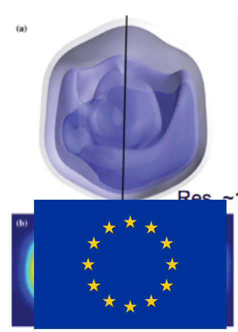


- Coherent imaging of biological samples with femtosecond pulses at the FLASH FEL: Manuco et al., New J. Physics **12**, 035003 (2010)



- Three-Dimensional Reconstruction of the Giant Mimivirus Particle with an X-Ray FEL: Ekeberg et al., PRL **14**, 098102 (2015)





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Why we want the 3D structure

Artists: Tim Nobel & Sue Webster

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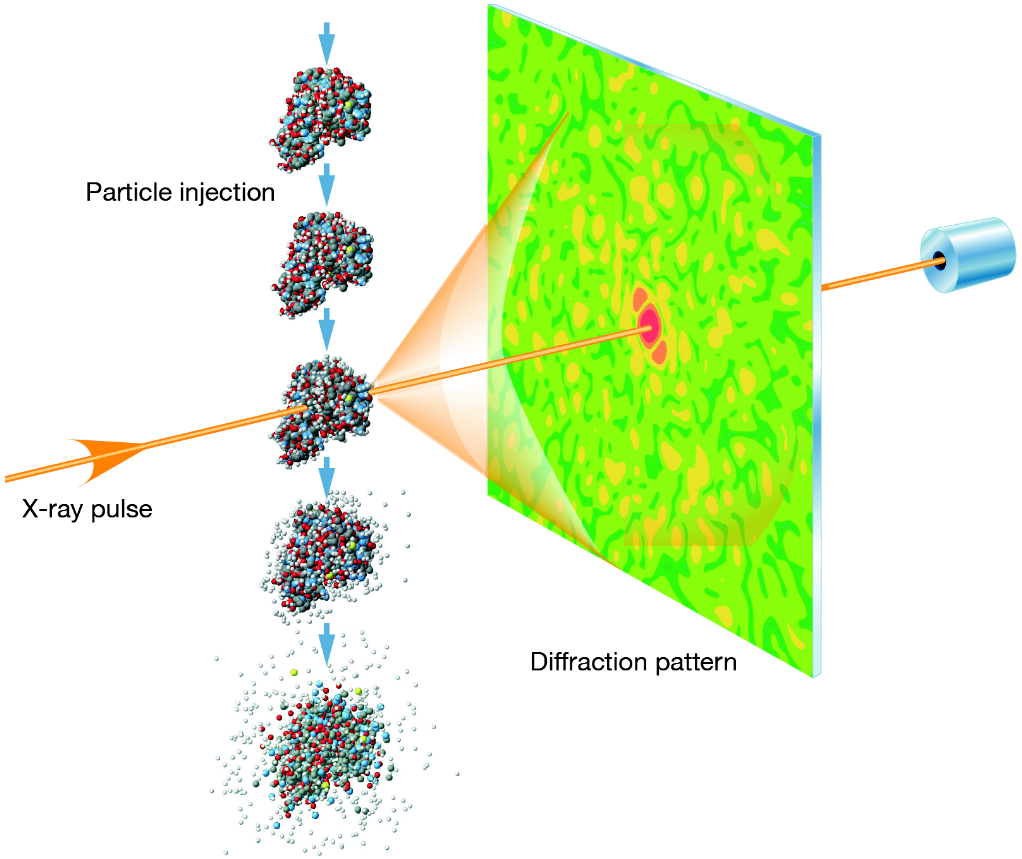
Single Particle Coherent Diffractive Imaging

3D comes for free

- A sample injector provides one molecule at a time in the interaction region.
- Each molecule arrives in an unknown orientation → 3D sampling
- Coherent x-ray photons scatter from the molecule
- Scattered photons are collected in a pixel area detector
- 2D patterns are merged into a 3D diffraction volume.
- Phase retrieval algorithms reconstruct the 3D electron density map



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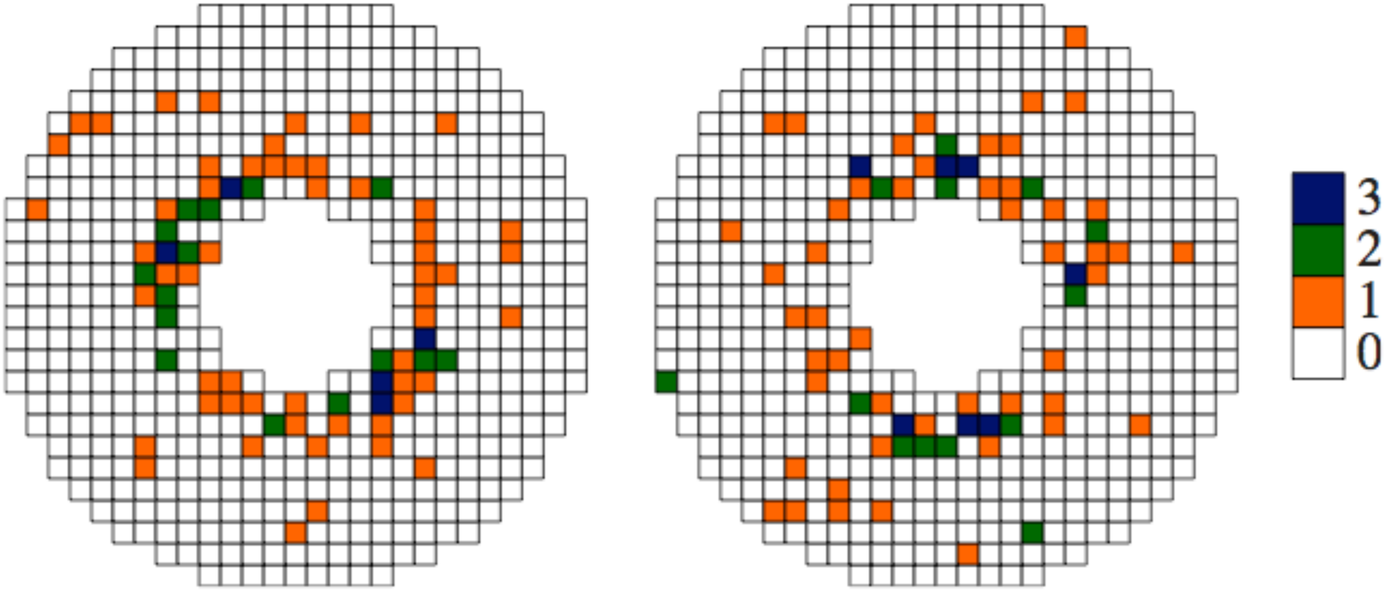
The orientation problem



"Are the photon counts different because the molecule presented a different orientation to the x-ray beam; is the difference attributable to the statistics of a shot-noise limited signal; or does some combination of the two apply?"

N. Loh and V. Elser, Phys. Rev. E, **80**, 026705 (2009).

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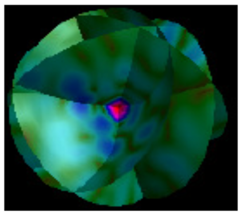
EMC: orientation of 2D patterns into 3D volume

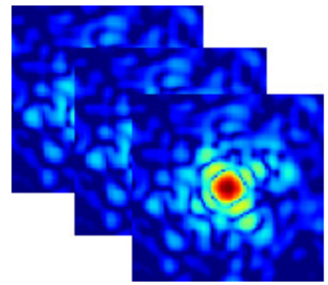
3D model $W_i(\mathbf{p})$



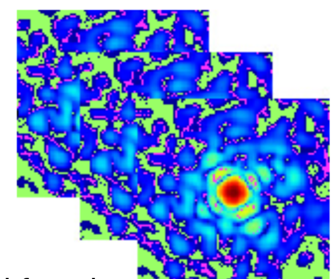
random initialization

Expansion

Model tomographs W_{ij}



Measurements K_{ik}



Compression

$$\mathbf{M}: W_{ij} \rightarrow W'_{ij} = \frac{\sum_{k=1}^{M_{\text{data}}} P_{jk}(W) K_{ik}}{\sum_{k=1}^{M_{\text{data}}} P_{jk}(W)}$$

normalized likelihood function

Maximization

$$W_{i+1}(\mathbf{p}) = \mathrm{C} \cdot \mathrm{M} \cdot \mathrm{E} \cdot W_i(\mathbf{p})$$

N. Loh and V. Elser, Phys. Rev. E, **80**, 026705 (2009).

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Konijnenberg, S. Advanced Optical Technologies, 6, 423 (2017)

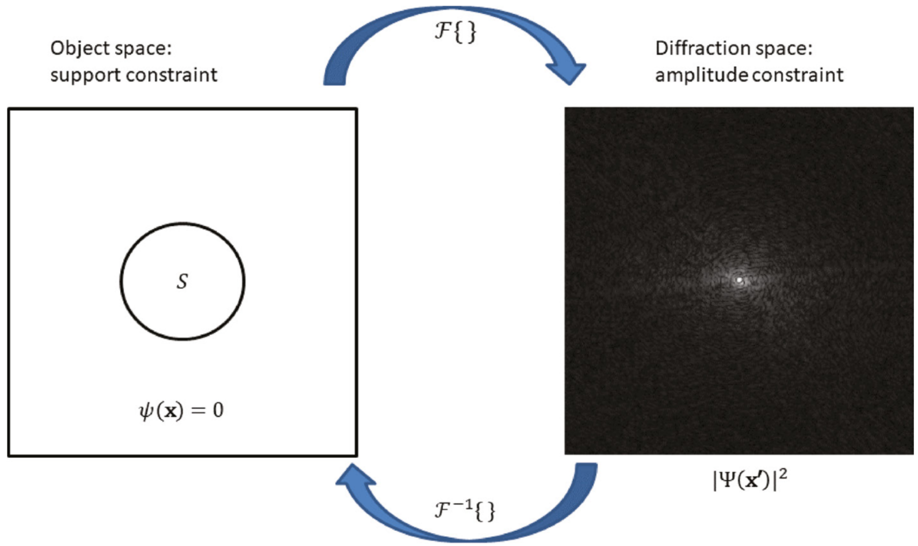
The phase problem

- Scattering phase is lost in the intensity measurement

$$I_c(q/2,\Omega) = \Omega \frac{d\sigma_T(\theta)}{d\Omega} \int_{-\infty}^{\infty} I_i(t) \left(|F_c(q/2,t)|^2 + S_c(q/2,t) + N_c^{free}(t) \right) dt$$

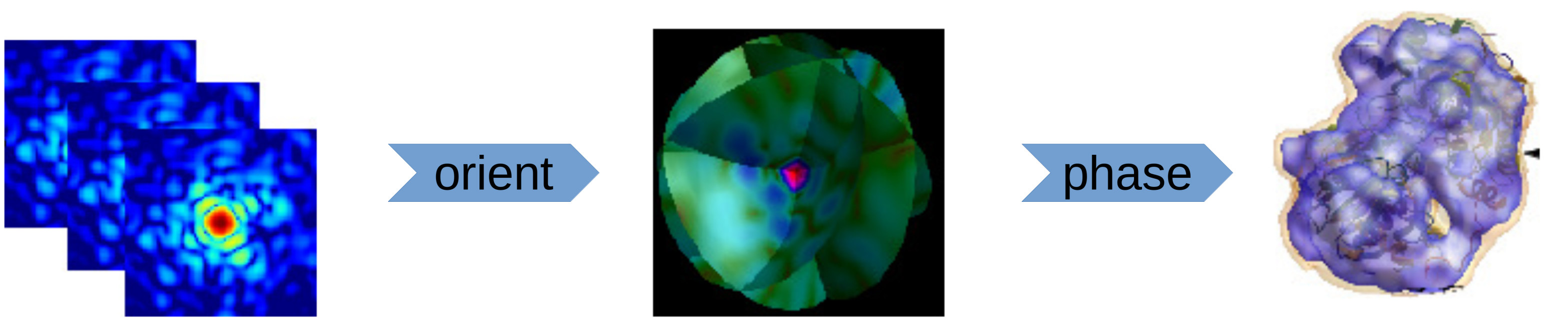
$$F_c(\vec{q},t) = \int d^3\vec{r}\, n(\vec{r},t)\, \mathrm{e}^{-i\vec{q}\cdot\vec{r}} = |F_c(\vec{q},t)|\ \mathrm{e}^{i\Phi(\vec{q},t)}$$

wanted measured ??



Implementation: libspimage, Hawk GUI

F. Maia et al., J. Appl. Cryst. **43,** 1535 (2010)



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Orientation and phasing are sensitive to experimental artifacts

- X-ray source properties (spatial, temporal, spectral, stochastics)
- X-ray optics imperfections (e.g. mirror height profile)
- Electronic radiation damage processes
- Detectors (nonlinear gain, noise, e-h plasma effects at high intensities)

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Simulations can help address these questions

- Study how each imperfection affects measurable quantities **in isolation**
- Look at combined effect of **entire experimental setup**

  ⇒ **Start-to-end experiment simulations**
- Systematic exploration of parameter space

And more:

- Serve beamline users and operators to optimize configurations
- Complement data analysis (combine forward simulation with inversion algorithms)

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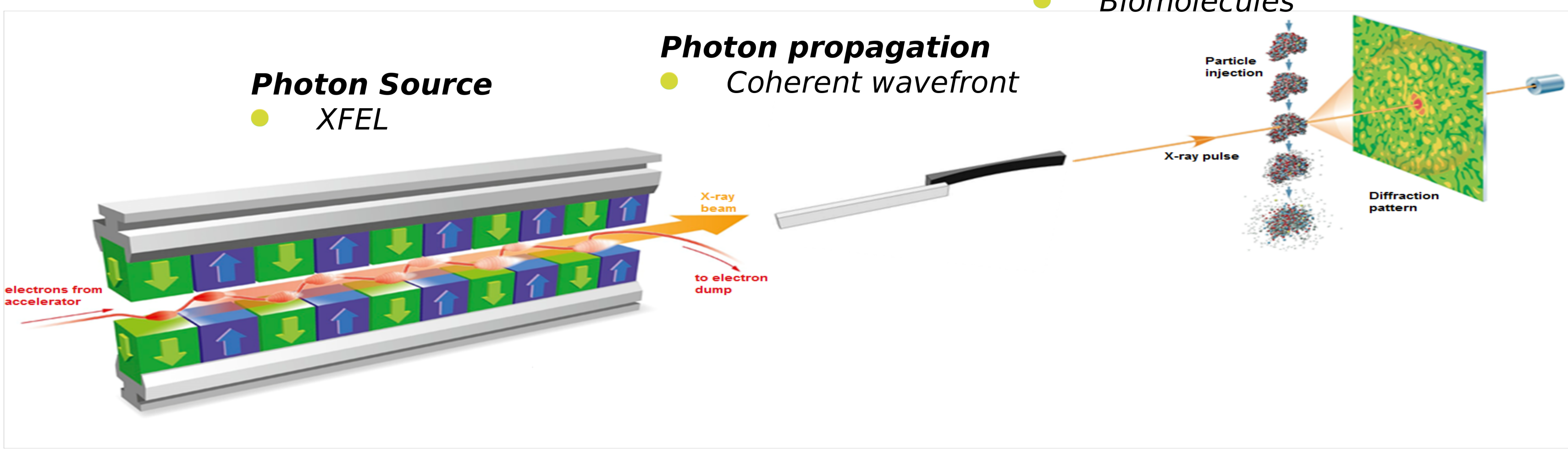
Our simulation tools facilitate complete “source – to – detector” simulations of SPB-SFX experiments

simS2E: The prototype for SIMEX

Yoon et al. Scientific Reports **6** 24791 (2016)

Signal generation
- *Diffraction*

Target/Sample
- *Biomolecules*



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SIMEX supports start-to-end simulation of various types of photon experiments at various light sources

Yoon et al. Scientific Reports **6** 24791 (2016)

Fortmann-Grote et al. Proc. NOBUGS 2016, 29 (2016)

Fortmann-Grote et al. Proc. SPIE, 2017, 102370S-34

Photon Source

- *XFEL*
- *Synchrotron*
- *Optical Laser*
- *Pump-probe*

Photon propagation

- *Fully coherent*
- *Raytracing*
- *Hybrid*

Signal generation

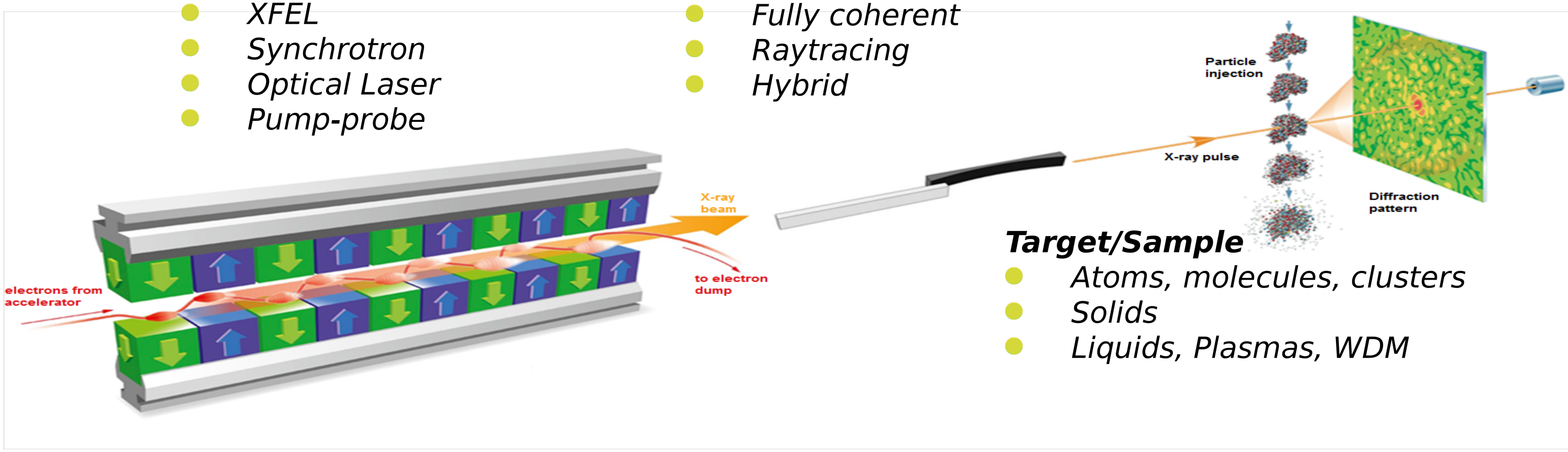
- *Spectroscopy*
- *Diffraction*
- *Inelastic scattering*

Detector response

- *Pixel detectors*

Target/Sample

- *Atoms, molecules, clusters*
- *Solids*
- *Liquids, Plasmas, WDM*



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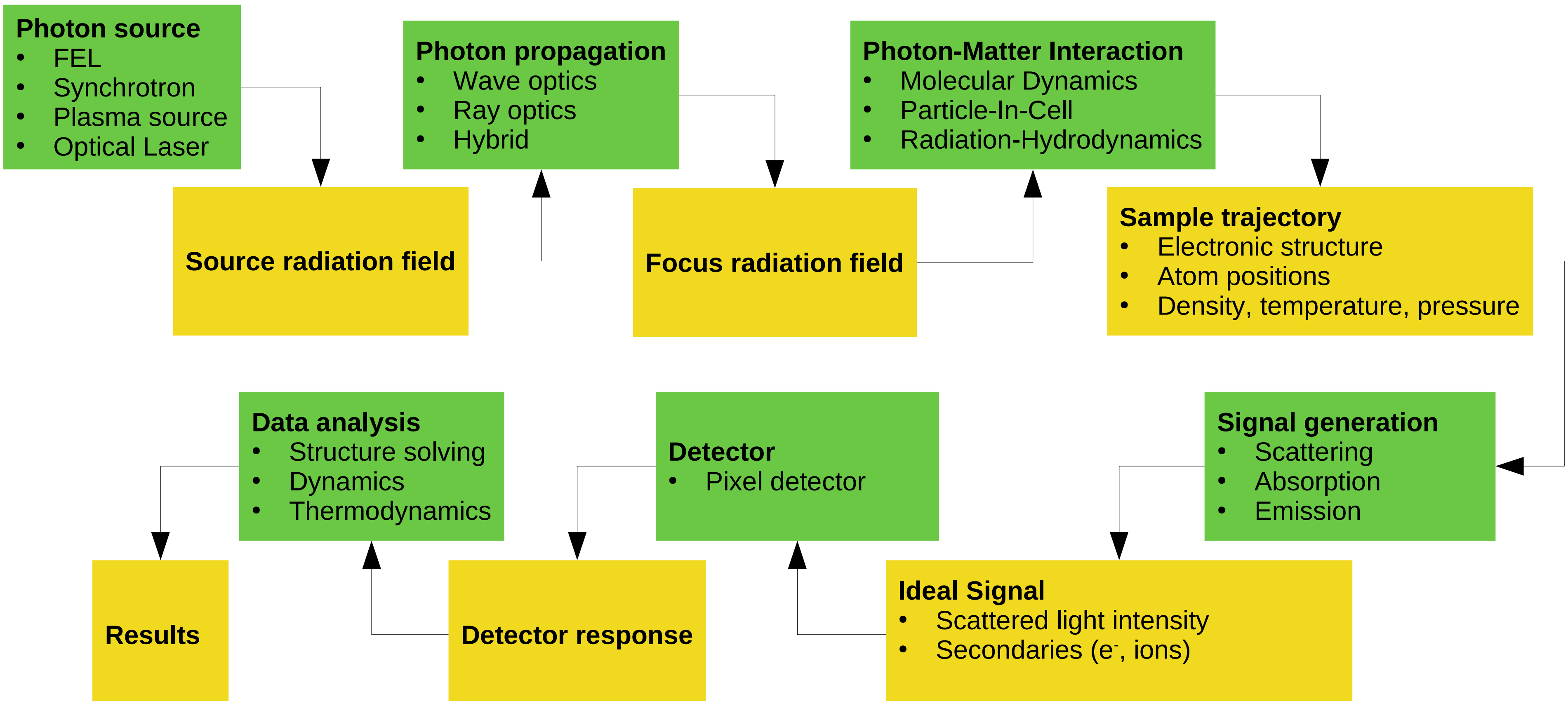
SIMEX provides user interfaces and data formats for start-to-end photon experiment simulations



Calculators: python APIs to advanced simulation codes
Data interfaces using metadata standards

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Interfaced simulation codes

X-ray source	FEL FEL Synchrotron	FAST Genesis/Ocelot Oasys	Yurkov, Schneidmiller (DESY) S. Reiche / G. Geloni et al. L. Rebuffi, M. Sanchez-Rio
Propagation	coherent wavefront prop. x-ray tracing	WPG/SRW Oasys	Samoylova, Buzmakov, Chubar L. Rebuffi, M. Sanchez-Rio
X-ray photon matter interaction	Atoms, molecules, clusters	XMDYN & XATOM	Z. Jurek et al. (CFEL)
		MCMD	P. Ho et al (ANL)
		HF/LDA	H. Quiney et al. (U Melbourne)
Optical photon matter interaction	1D Rad-Hydro 2D Rad-Hydro 3D PIC	Esther Multi2D PIConGPU	Colombier et al. (CEA) R. Ramiz et al. M. Bussmann et al. (HZDR)
Signal generation	molecule, cluster scattering Plasma SAXS Plasma Compton/Thomson Crystal diffraction EXAFS	SingFEL paraTAXIS XRTS CrystFEL/pattern_sim FEFF8L	C.H. Yoon (LCLS) T. Kluge et al. (HZDR) G. Gregori, CFG T. White et al. (CFEL) J.J. Rehr et al. (U Washington)
Detector simulation	2D Pixel detectors	X-CSIT, Karabo	T. Rüter et al. (XFEL)
Analysis/Reconstruction	Pattern orientation Phasing	EMC DM	N.D. Loh (Singapore)

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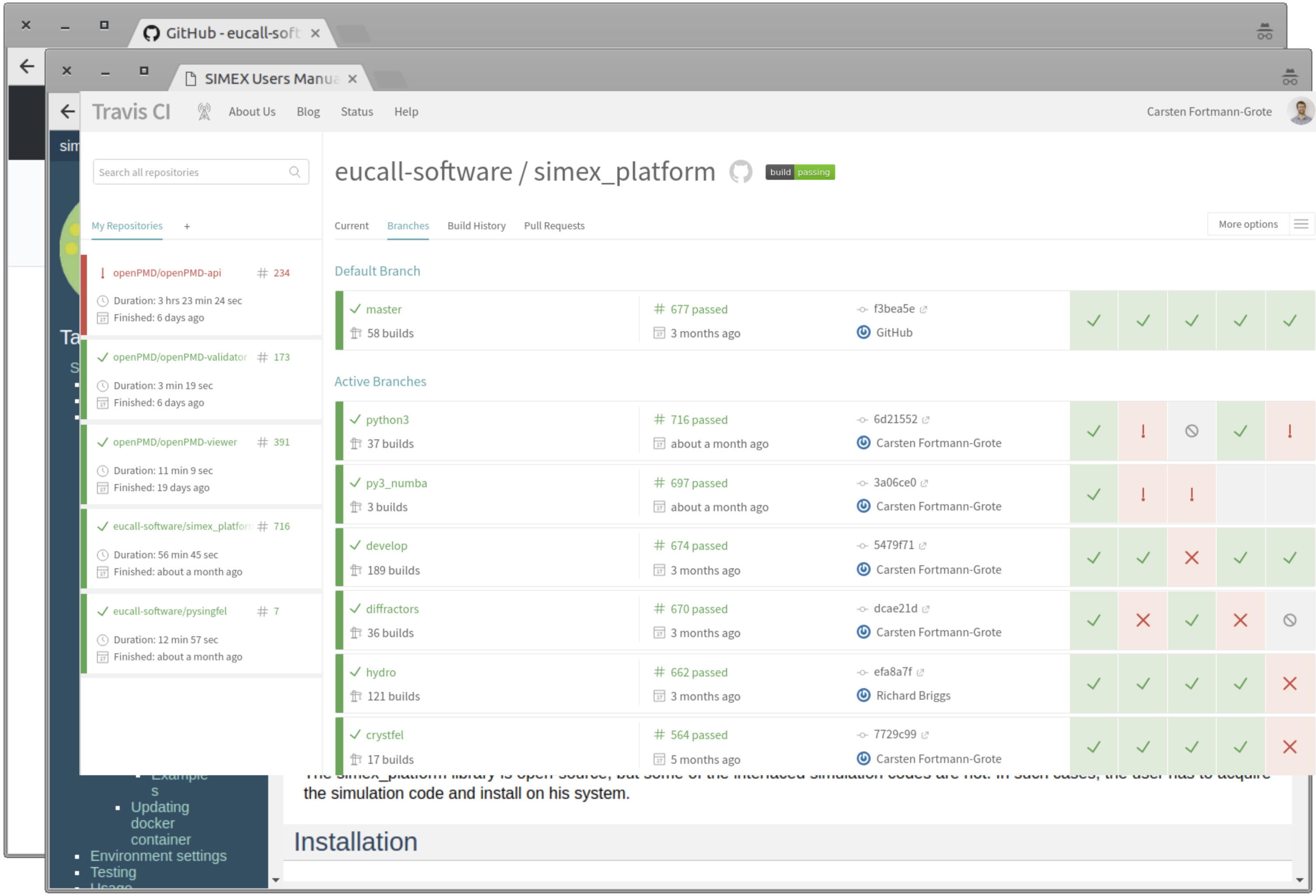
SIMEX is developed as a GPL'ed open source project



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An example:
Simulation of single-particle imaging at SPB-SFX

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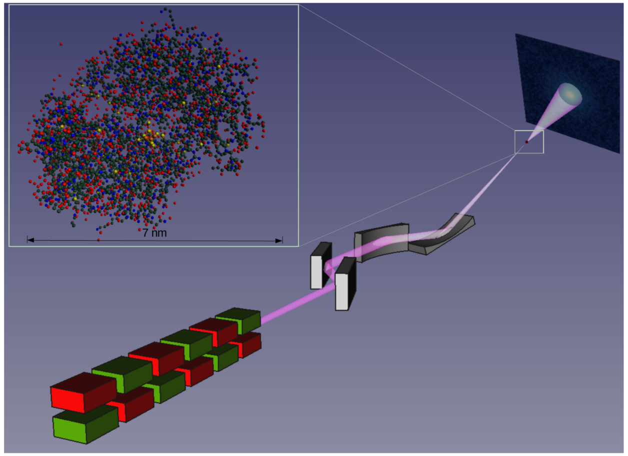
The test case: SPI of 2NIP with 5 keV photons at SPB-SFX

FEL Source

- **Pulse duration 3 fs, 9 fs, 30 fs**
- Photon energy 4.96 keV

Sample

- Two-nitrogenase protein (2NIP)
- ~5000 non-H atoms 🕮 Schlessman et al. J. Mol. Biology (1998)
- Iron-Sulfur ligand “SF4“
- Known crystallographic structure



Beamline optics

- Pair of offset mirrors
- KB nano-focussing
- Mirror height profiles included

Simulation

- 40 pulses from FAST XFEL Pulse Database
- Propagation: WPG (SPB-SFX beamline)
- PMI: ~1000 Sample trajectories 100 snapshots per trajectory
- Apply random rotation of atom coordinates to each trajectory
- 200 diffraction patterns per trajectory

  → 200000 patterns

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XFEL Source Simulations – FAST Code

Saldin et al. NIMP **A429**, 233 (1999)

- Resonance approximation

$$j_1(\boldsymbol{r},t) = \tilde{j}_1(\boldsymbol{r},t)\exp(\mathrm{i}\omega(z/c - t)) + \mathrm{C.C.}$$
$$E(\boldsymbol{r},t) = \tilde{E}(\boldsymbol{r},t)\exp(\mathrm{i}\omega(z/c - t)) + \mathrm{C.C.}$$

- Self-consistent solutions of electric field and current density in resonance approximation

$$\tilde{E}(z,\boldsymbol{r}_\perp,t) = \mathrm{i}\frac{\omega}{c^2}\int_0^z \frac{\mathrm{d}z'}{z-z'}\int \mathrm{d}\boldsymbol{r}_\perp \tilde{j}_1\left(z',\boldsymbol{r}'_\perp,t-\frac{z-z'}{c}\right)\exp\left[\frac{\mathrm{i}\omega|\boldsymbol{r}_\perp - \boldsymbol{r}'_\perp|^2}{2c(z-z')}\right]$$
$$\frac{d\boldsymbol{P}}{dt} = q(\tilde{\boldsymbol{E}} + \boldsymbol{V}\times\tilde{\boldsymbol{B}})$$

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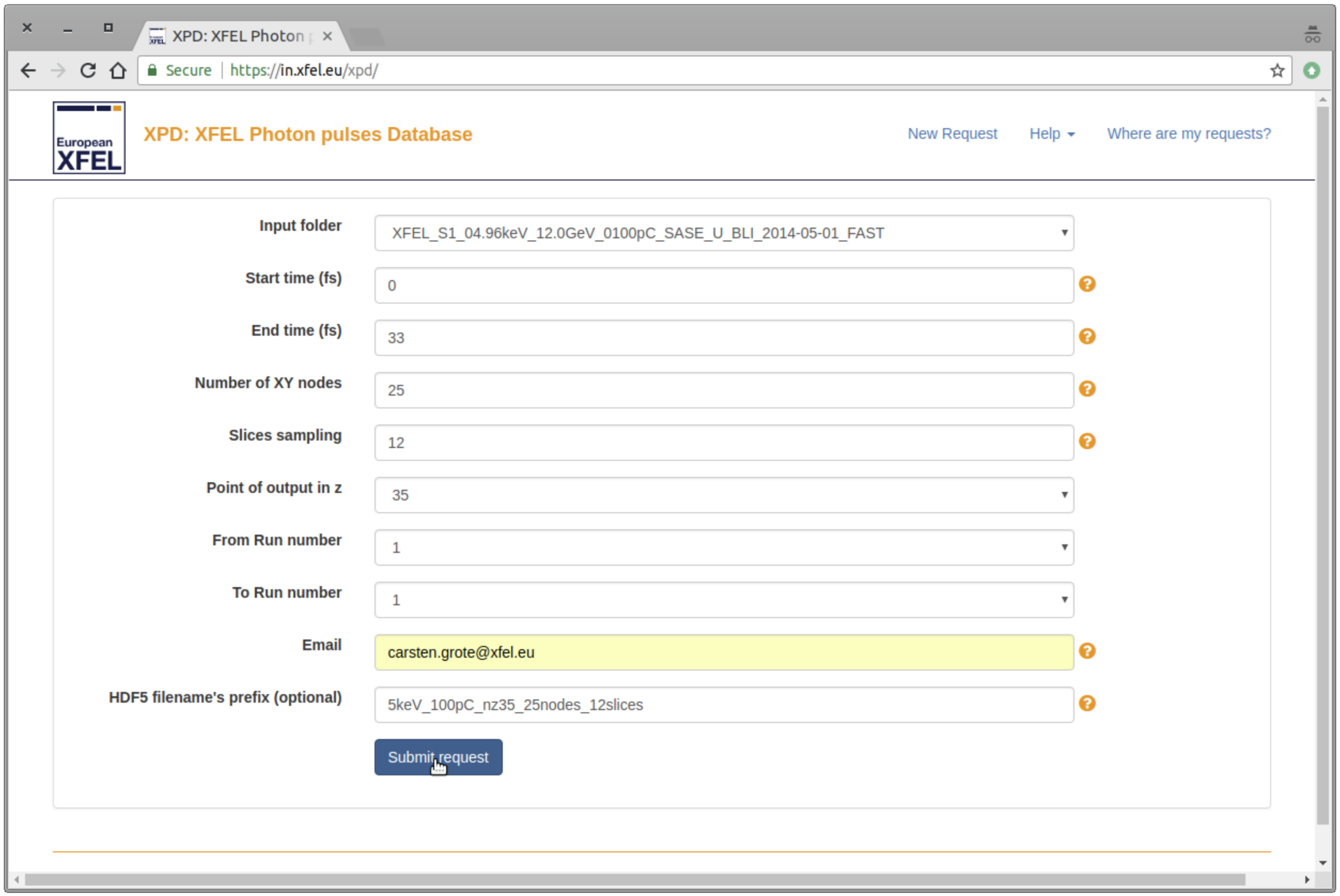
The XFEL Pulses Database serves precomputed SASE pulses



- FLASH @ 84 eV
- XFEL SASE1
  - 5.0 keV
  - 8.9 keV
  - 12.4 keV
  - 24.8 keV
- XFEL SASE3
  - 0.53 keV
  - 0.71 keV
  - 0.77 keV
  - 0.80 keV
  - 1.18 keV

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Coherent Wavefront Propagation

implemented in SRW (github.com/ochubar/SRW) 🕮 Chubar et al. NIMP **A593**, 30 (2008)

python interface: WPG (github.com/samoylv/WPG) 🕮 Samoylova et al. J. Appl. Cryst. (2016)

- Huygens-Fresnel convolution integral

$$E_\perp(x_2, y_2, \omega) \simeq \int\int \mathrm{d}x_1\, \mathrm{d}y_1\, \boldsymbol{K}(x_2, y_2, x_1, y_1, \omega)\, E_\perp(x_1, y_1, \omega)$$

- Free – space propagation

$$\boldsymbol{K}(x_2, y_2, x_1, y_1, \omega) \simeq -\frac{ik}{2\pi z} \exp\left\{\frac{ik}{2z}\left[(x_2 - x_1)^2 + (y_2 - y_1)^2\right]\right\}$$

- Thin optical elements (thin lense, CRL)

$$\boldsymbol{K}(x_2, y_2, x_1, y_1, \omega) = \boldsymbol{T}(x_1, y_1, \omega)\, \delta(x_1 - x_2)\, \delta(y_1 - y_2)$$

- Thick optical elements (e.g. grazing incidence mirror)

$$\boldsymbol{K}(x_2, y_2, x_1, y_1, \omega) \cong \boldsymbol{G}(x_1, y_1, \omega) \times \exp\left[(i\omega/c)\, \Lambda(x_2, y_2, x_1, y_1, \omega)\right] \times \delta[x_1 - \tilde{x}_1(x_2, y_2) \ldots (x_2, y_2)]$$

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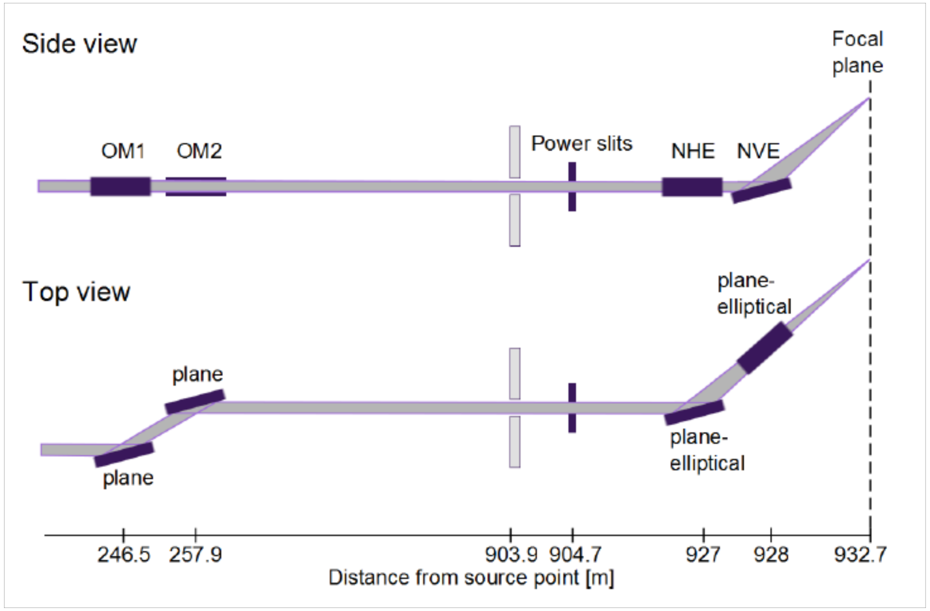
Wavefront propagation from SASE1 Undulator to SPB-SFX upstream interaction region



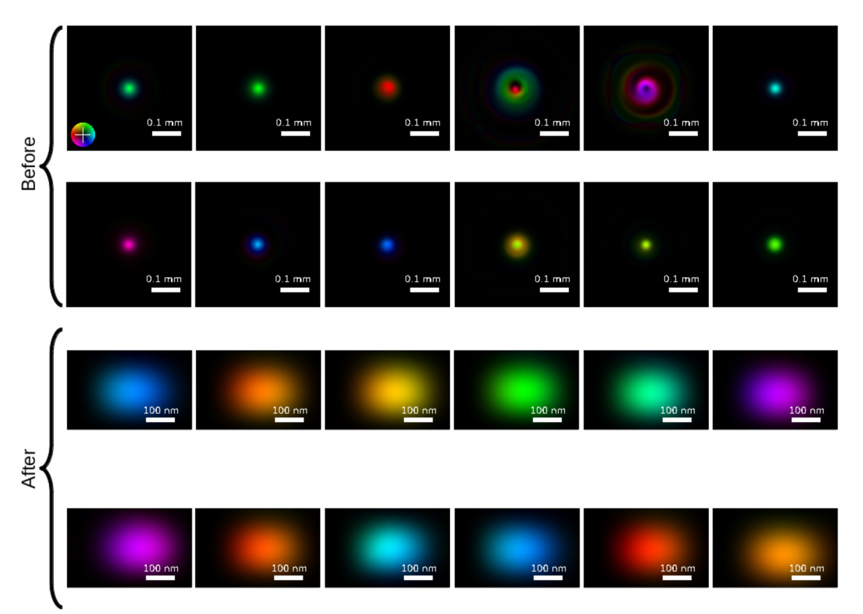


Figure 6. Intensity and phase maps of the SASE FEL X ray slices in a 9 fs pulse before and after propagating through the optics. The phase is color-coded. The distances between slices are about 0.2 fs.

Yoon et al. Scientific Reports **6** 24791 (2016)

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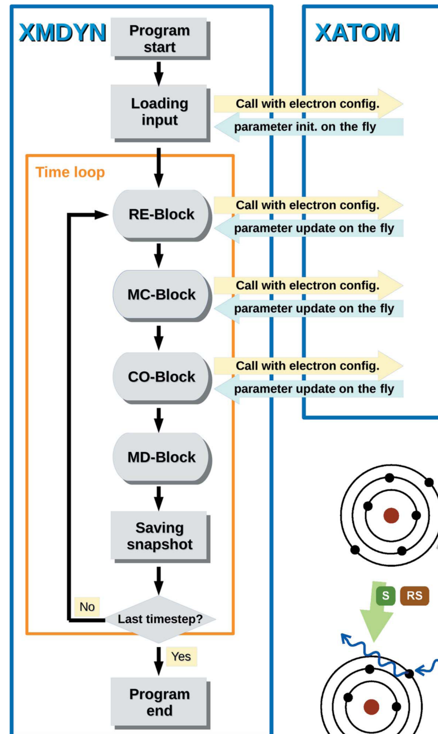
Radiation-matter interaction: XMDYN & XATOM

Jurek et al. J. Appl. Cryst. (2016)

Son et al. Phys. Rev. A **83**, 033402 (2011)

- Ions move according to Newtonian mechanics
- Monte–Carlo simulation for electronic transitions according to rates/cross-sections from
- Hartree-Fock-Slater electronic structure code (XATOM)
- Output:
  - Atom positions $R_i(t)$
  - form factors f(**k**,t)
  - structure factors S(**k**, t)



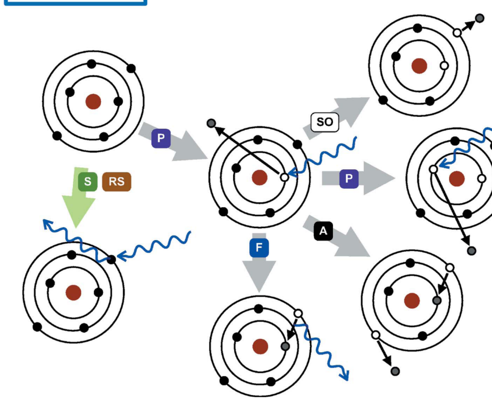
$$[-\tfrac{1}{2}\nabla^2 + V(\mathbf{r})]\psi(\mathbf{r}) = \varepsilon\psi(\mathbf{r})$$

$$V(\mathbf{r}) = -\frac{Z}{r} + \int \frac{\rho(\mathbf{r})}{|\mathbf{r}-\mathbf{r}'|}d^3r' - \frac{3}{2}\left[\frac{3}{\pi}\rho(\mathbf{r})\right]^{1/3}$$

$$\rho(\mathbf{r}) = \sum_{i\in I}\psi_i^\dagger(\mathbf{r})\psi_i(\mathbf{r})$$

$$\frac{d}{dt}P_I(t) = \sum_{I'\neq I}^{\text{all config.}} [\Gamma_{I'\to I}P_{I'}(t) - \Gamma_{I\to I'}P_I(t)]$$

$$\Gamma_{I\to I'} = \frac{2\pi}{\hbar}\left|\langle\psi_{I'}\left|H_{\text{rad}}\right|\psi_I\rangle\right|^2$$



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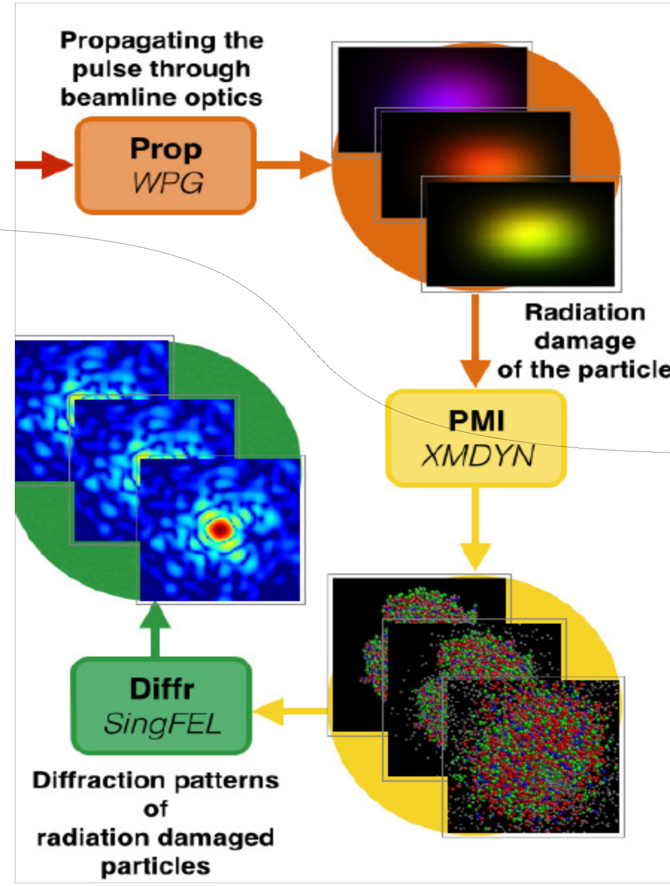
Diffraction

$$I_c(q/2,\Omega) = \Omega \frac{d\sigma_T(\theta)}{d\Omega}\int_{-\infty}^{\infty} I_i(t)\left(|F_c(q/2,t)|^2 + S_c(q/2,t) + N_c^{free}(t)\right) dt$$

- Coherent scattering from bound electrons
- Incoherent (Compton) scattering from bound electrons
- Compton scattering from free electrons



$E(\mathbf{r},t)$

$\ast$

$\mathbf{R}_i(t)$

$f(\mathbf{k},t)$

$S(\mathbf{k},t)$

Yoon et al. Scientific Reports **6** 24791 (2016)

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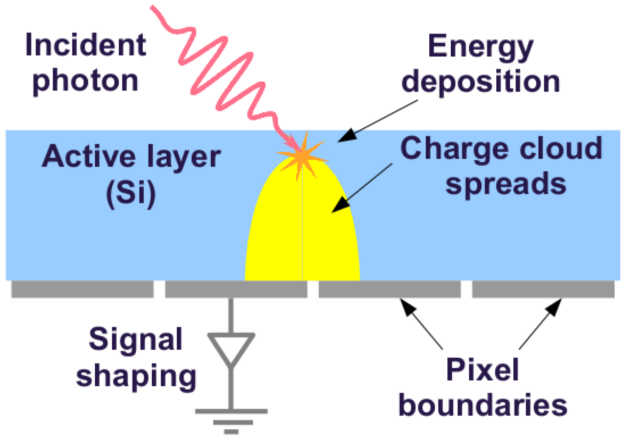
Detector Simulations

Divide the radiation detection process into three stages:

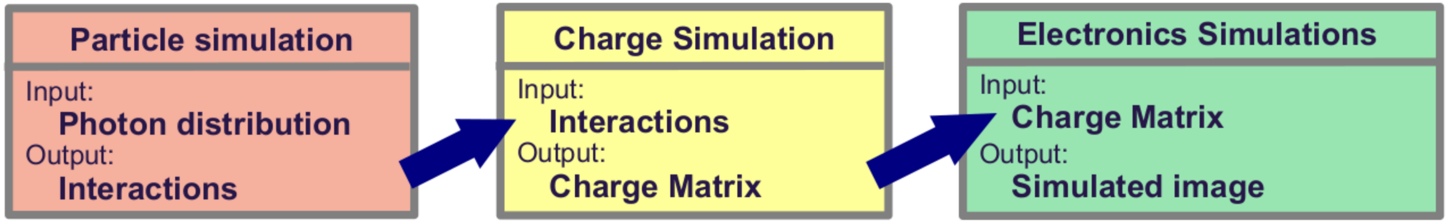


X-ray/matter interaction
- Energy deposition in the detector material
- Based on Geant4 v10.0, using Livermore models based on Evaluated Photon Data Library (EPDL)
- Validation for previous versions exist (Pia & Batic et al., nano5, 2009, 2012, 2013)

Charge carrier transport
- Drift due to bias voltage, lateral diffusion
- Carriers accumulate to a measurable signal

Detector electronics
- Amplify and shape the signal Electronics Simulation
- Phenomenological approach

Simulations run in individual devices in Karabo. Together they form a **X-ray Detector Simulation Pipeline**.



Joy et al. J. Instr. **10** (2015)
Rüter et al. IEEE Conf. Nuclear Science Symposium 2015 (2016)

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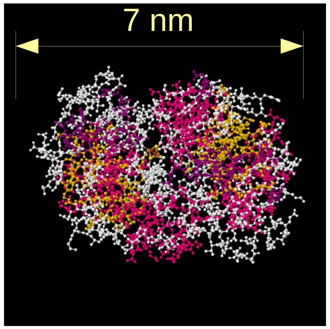
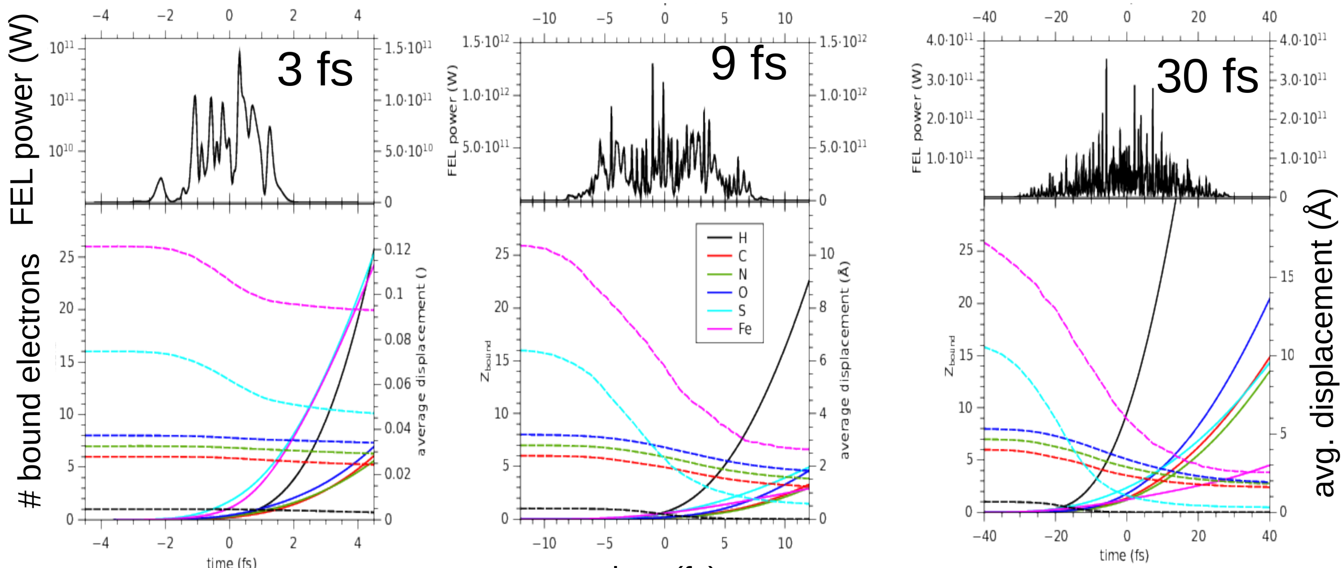


sample molecule 2NIP

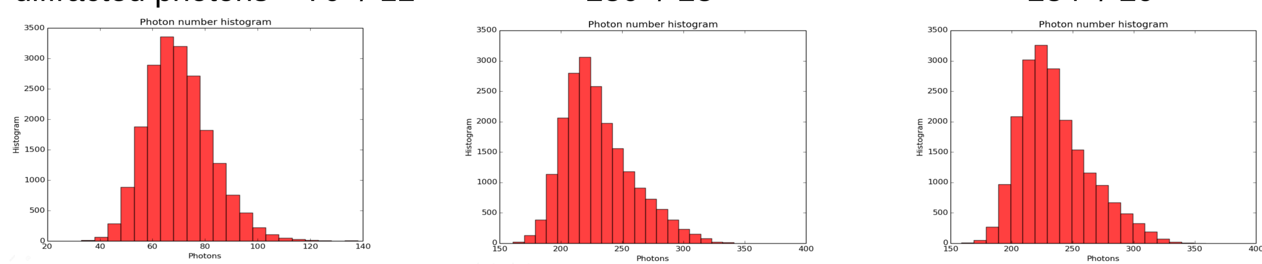
Atom	τ_{Auger}(fs)
C	10.7
N	7.1
O	4.9
S	1.3
Fe	2.0

photons per pulse = $1\cdot10^{11}$ $5\cdot10^{11}$ $1\cdot10^{12}$



time (fs)

diffracted photons = 70+/-12 230+/-28 234+/-29



CFG et al., IUCrJ (2017)

Yoon et al. Scientific Reports **6** 24791 (2016)

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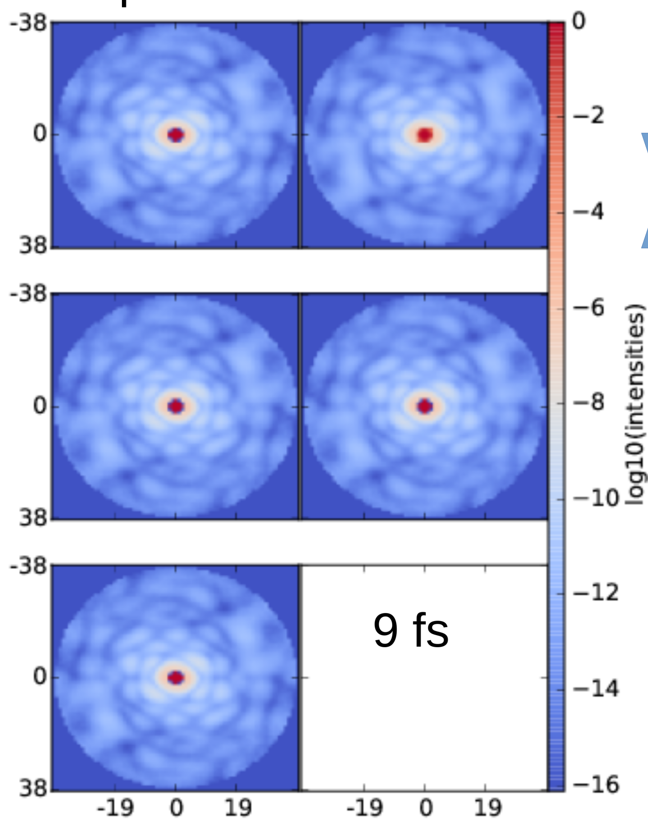
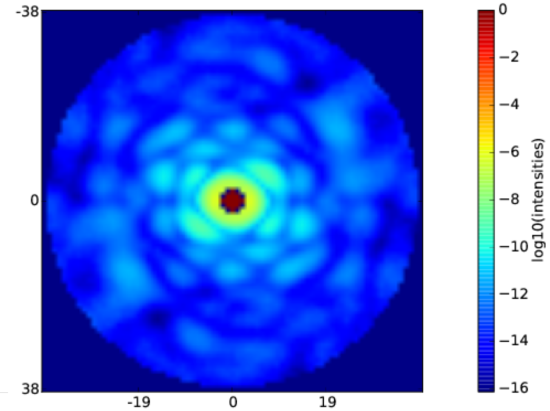
EUCALL

The coefficient of variation quantifies the consistency of the oriented 3D diffraction volume

5 independent orientation runs



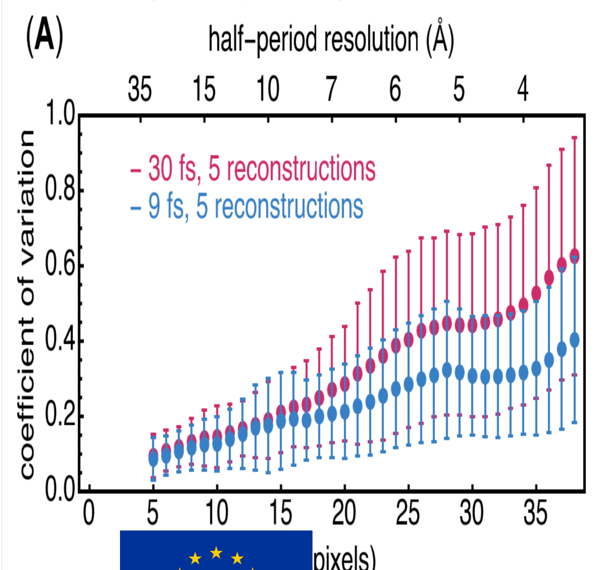
Average, rms



σ(**q**) = rms/average

$$\sigma(\mathbf{q}) = \frac{\sqrt{\left\langle \left| I_n(\mathbf{q}) - \langle I_n(\mathbf{q})\rangle_n \right|^2 \right\rangle_n}}{\langle I_n(\mathbf{q})\rangle_n}$$

radial projection



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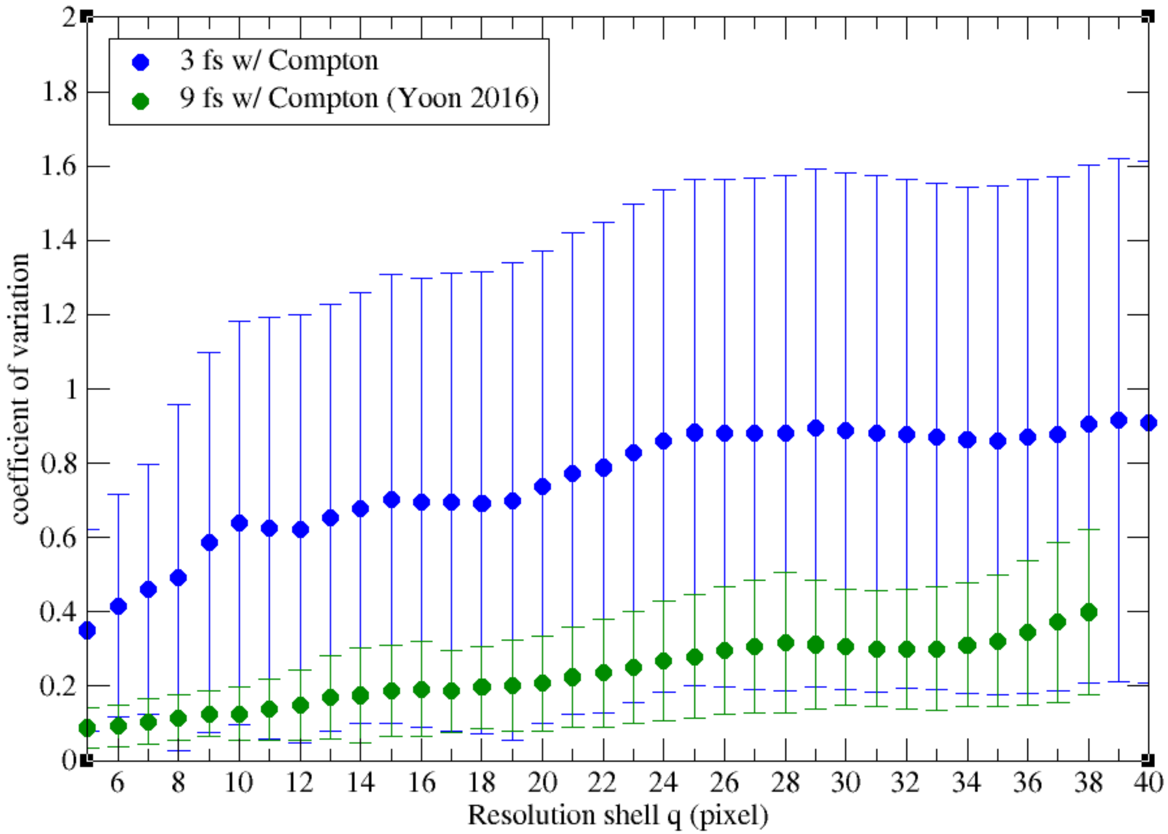
Oriented 3 fs diffraction patterns show 2-3 times larger variation compared to 9 fs data



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Summary

- Coherent diffractive imaging is a powerful technique to resolve the molecular and atomic structure of various kinds of matter.
- Experiments at X-FELs have demonstrated “diffract-then-destroy” on structured targets, cells, and viruses
- Simulations support efforts to achieve sub-nm level resolution single-particle imaging.
- The simulation platform SIMEX facilitates simulation of a wide range of photon experiments at various light sources.
- Applications demonstrate the usability and usefulness of this simulation toolbox.
- Future developments target a tight integration of our simulation tools with data analysis frameworks (→ integrated analysis) and application in teaching and training.

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Thank you for your attention

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