

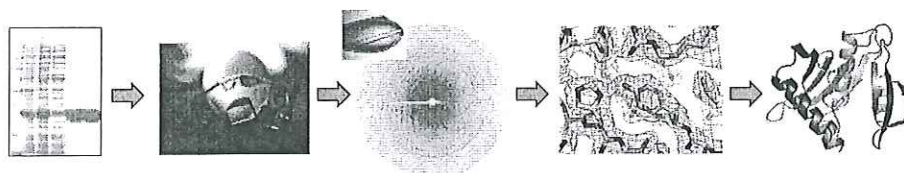
Synchrotron Application: Protein Crystallography

Nuttawan Pramanpol, PhD

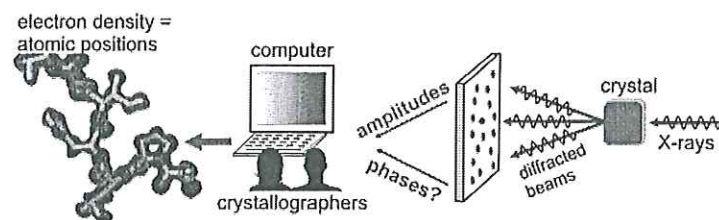
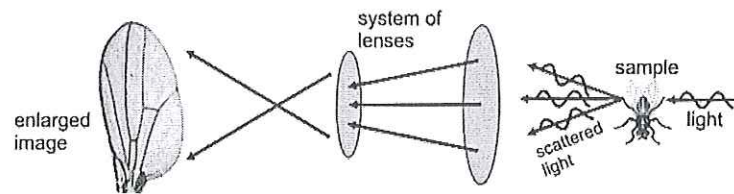
Email: nuttawan@slri.or.th

Protein Crystallography

**A commonly used technique to determine
the 3D structure of proteins at atomic resolution**

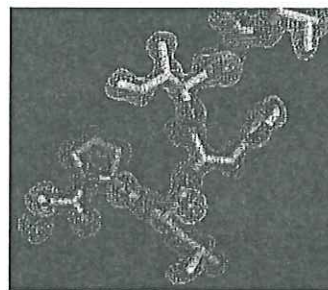
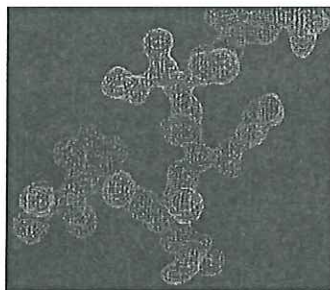


Protein Crystallography

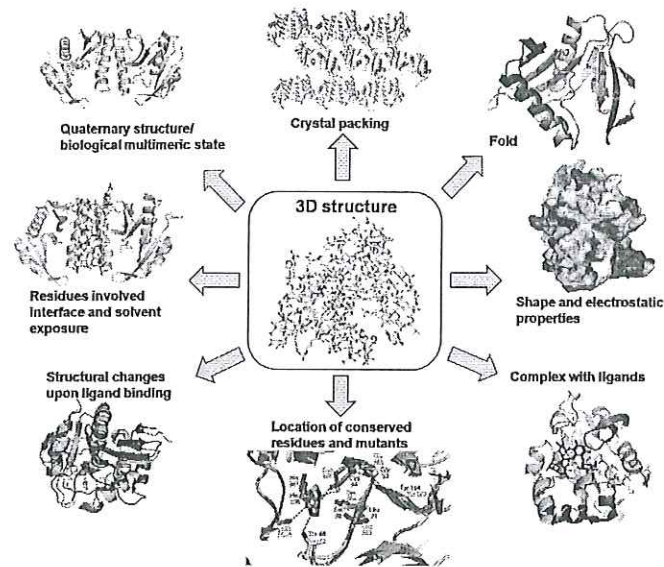


Interpretation of electron density

To interpret the electron density which is experimentally determined from the scattering of X-ray by electrons in the atoms of the protein molecule, the atomic structure is therefore built into the electron density map.



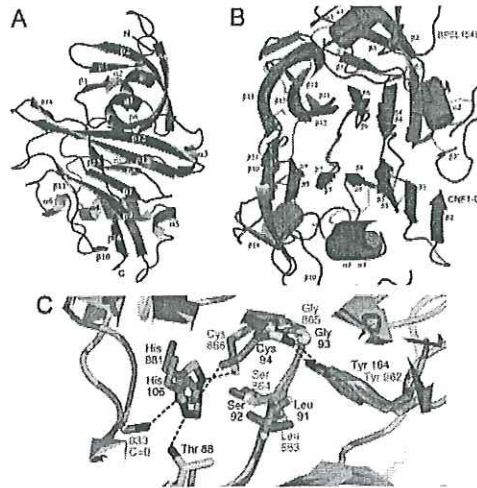
What 3D structures can do for you?



Applications

- Structural genomics
 - infer function from structure
- Enzyme Technology
 - protein engineering e.g. mutagenesis
 - enzyme complex with substrate, cofactor, coenzyme
- Pharmaceutical development
 - rationale drug discovery

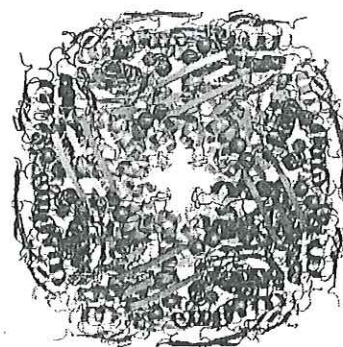
Applications



From an uncharacterized protein to be a novel toxin from *Burkholderia pseudomallei*

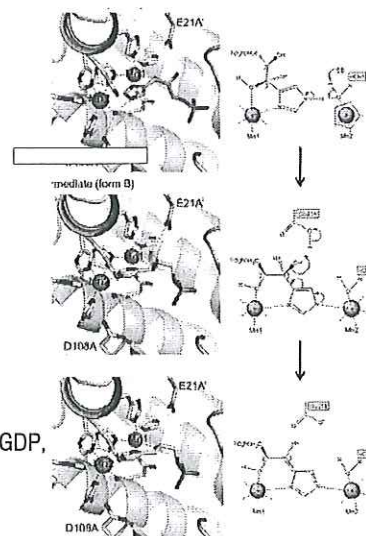
Cruz-Migoni A, et al. (2011) Science 334: 821-824

Applications

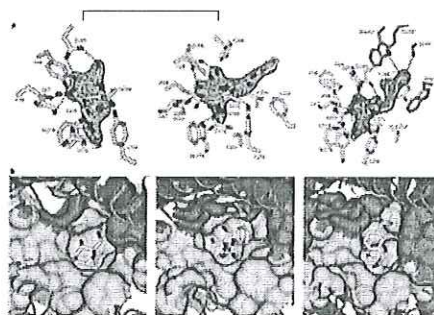
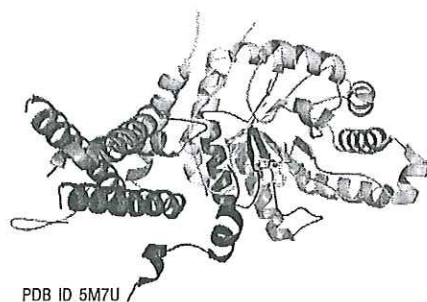


Crystal structures describe the reaction mechanism of IGDP, a potential herbicide target

Bisson et al. (2015) Structure 23: 1235-1245



Applications



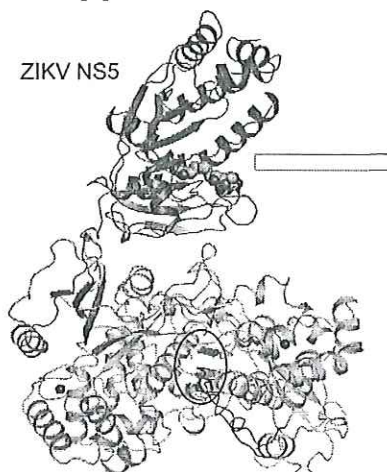
3D structure of human O-GlcNAc-hydrolase and inhibitors:

A hope for treating neurodegenerative diseases

Christian Roth et al. (2017) Structural and functional insight into human O-GlcNAcase, *Nat. Chem. Biol.* 13: 610-612

Applications

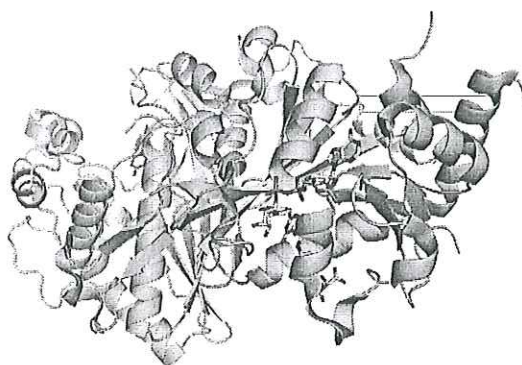
ZIKV NS5



Crystal structure of a key protein in Zika virus for anti-viral drug development

<https://phys.org/news/2017-03-key-protein-zika-virus.html>

Applications



Structural studies on dihydrofolate reductase-thymidylate synthase (DHFR-TR),
an anti malaria drug target

Yuthawong et al (2012) Proc Natl Acad Sci U S A 109 16823-16828

Protein Crystallography Facility in Thailand

Step	Availability
• Molecular cloning	University/Institute Labs
• Protein production and purification	University/Institute Labs
• Protein crystallization	MU, BIOTEC, SUT, KMUTT
• Conventional source X-ray diffraction	MU, BIOTEC, SUT
• Automated protein crystallization	Xtal Lab @SLRI only
• X-ray diffraction and data collection with tunable energy	BL7.2W: MX @SLRI only

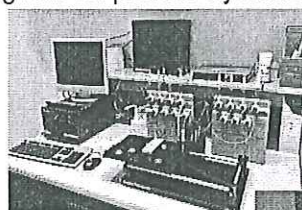
BL7.2W: MX



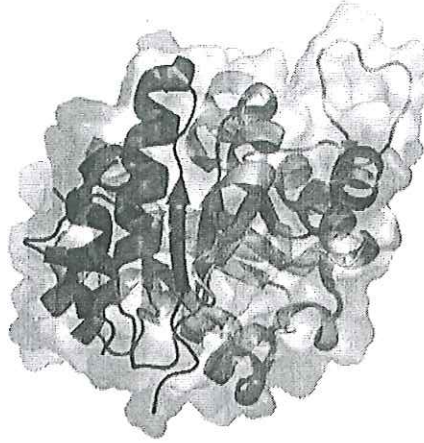
Protein crystallization facility(Xtal Lab)

A national central laboratory and a training hub for protein crystallization with an automated crystallization system

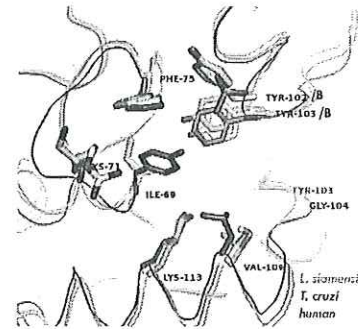
- Protein crystallization setup
 - Screening
 - Optimization
- Crystal manipulation
 - Crystal handling
 - Crystal storage
- Structural analysis (macOS)
 - CCP4 –Data processing
 - Phenix –Structure determination
 - ARP/wARP –Model building
 - Pymol –Visualization
 - QTMG



Highlight structure from our facility @SLRI



3D structure of triosephosphate isomerase
from *Leishmania siamensis* (PDB ID: 5CG7)



Kuaprasert et al. (2015) Suranaree J. Sci. Technol. 22(3):285-293

Achieved workshop/training

- ASEAN Synchrotron Science Camp @SLRI, Thailand
- ASEAN Workshop on Protein Crystallography @SLRI, Thailand
- Synchrotron Applications on Bioscience Training @SLRI, Thailand
- Protein Crystallography Workshop @MGI, Malaysia
- Protein Crystallization Training @WU, Thailand



