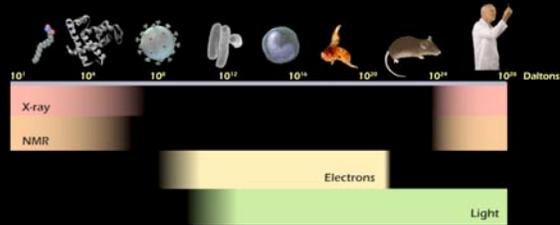


Visualizing Cells at Molecular Resolution

Sriram Subramaniam

Laboratory of Cell Biology
Center for Cancer Research
National Cancer Institute, NIH

Imaging gaps in biology and medicine



S. Subramaniam, Curr. Opin. Microbiol. (2005)

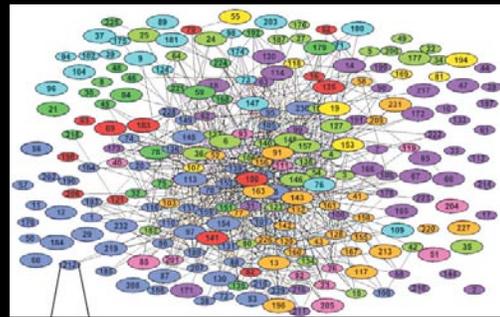
van Leeuwenhoek's
microscope



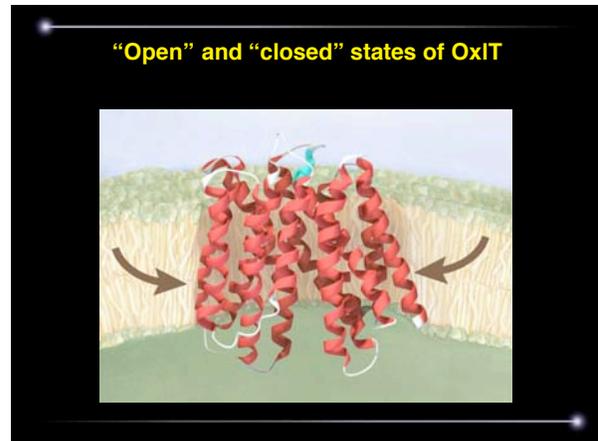
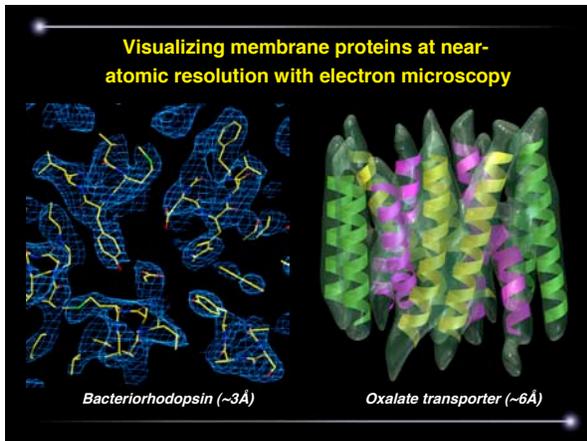
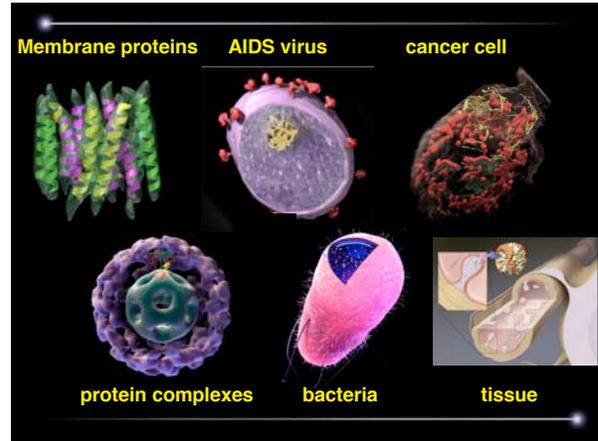
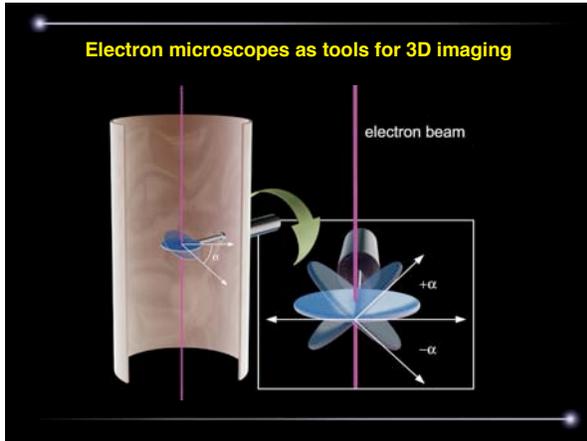
Modern electron
microscope



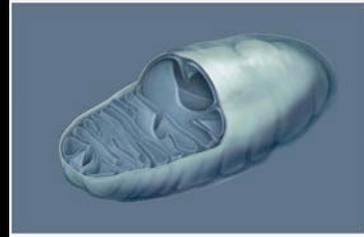
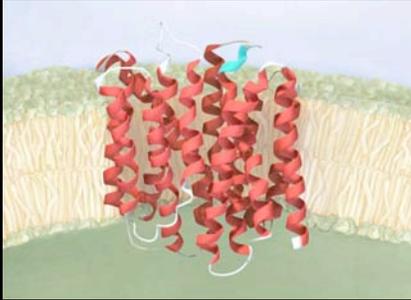
Protein networks & signaling pathways



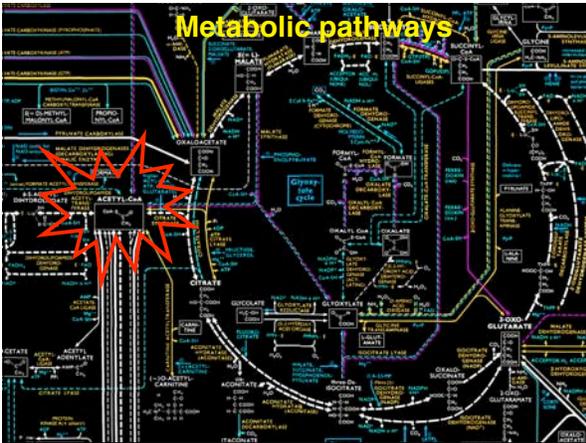
From Gavin, Ho and co-workers (2002)



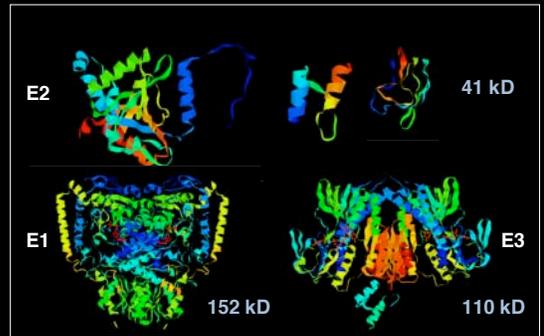
“Open” and “closed” states of OxIT



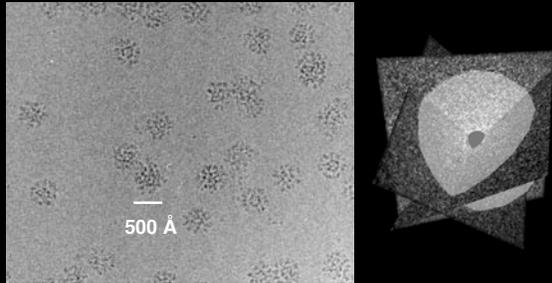
Metabolic pathways



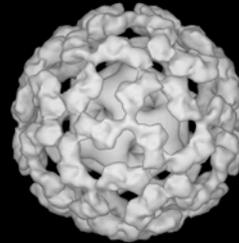
Components of the pyruvate dehydrogenase complex



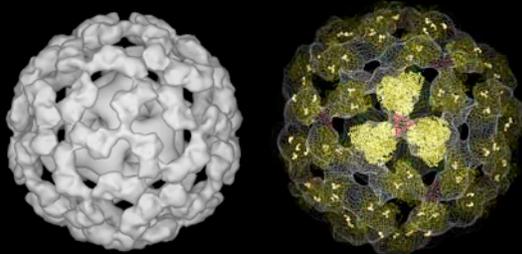
Images of single multi-enzyme complexes



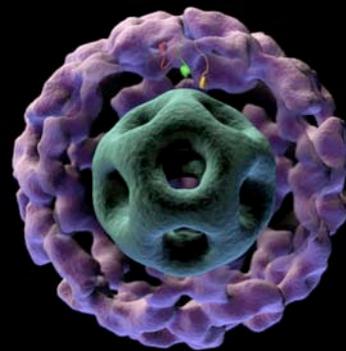
Reconstructed 3D structure....

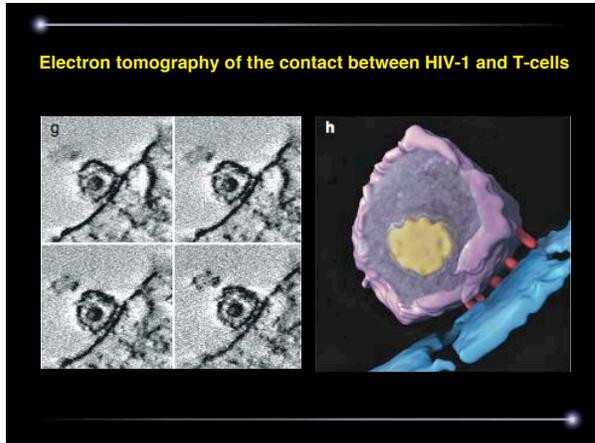
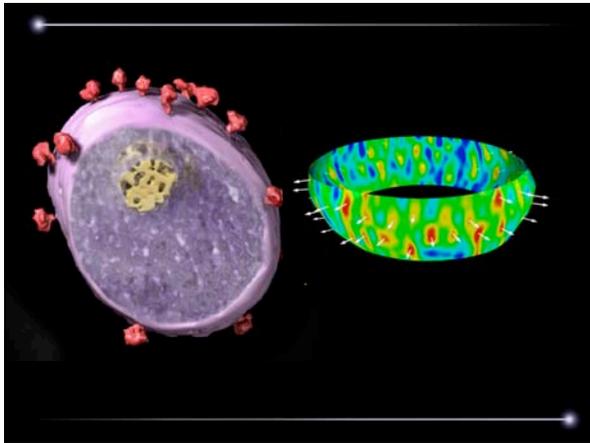
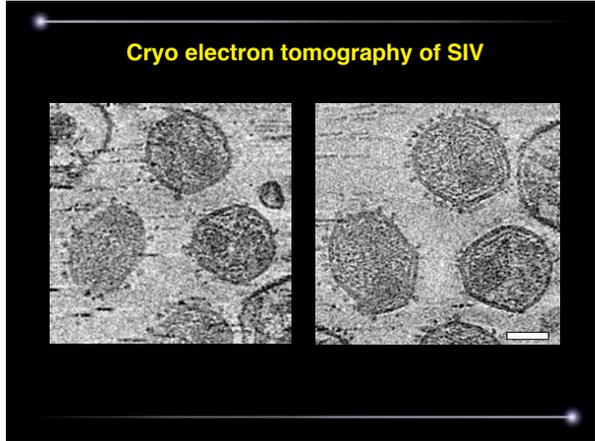
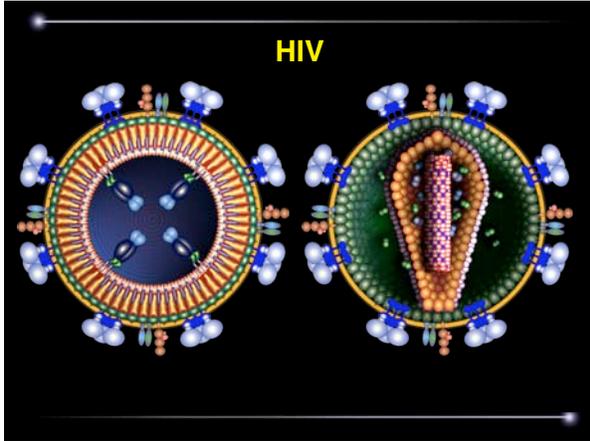


Reconstructed 3D structure....

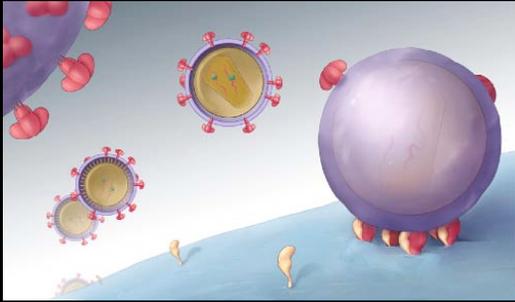


....and atomic interpretation





Catching HIV in the act

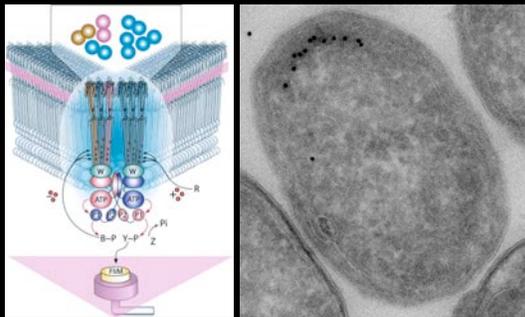


The signaling cascade in bacterial chemotaxis



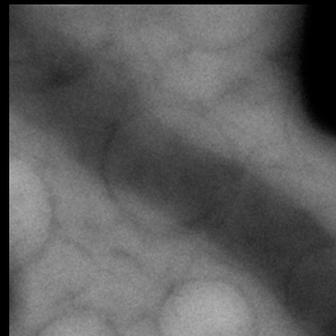
Robert MacNab and colleagues

The signaling cascade in bacterial chemotaxis

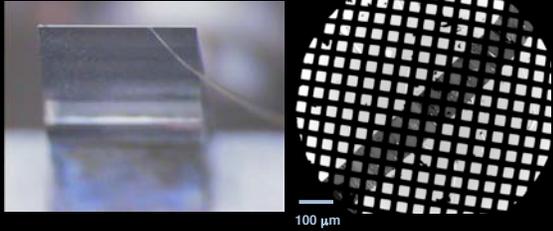


from Harshey et al (2003)

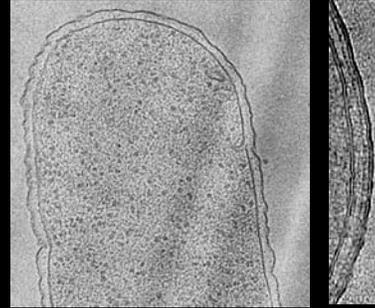
Low dose image of rapidly frozen *E.coli*



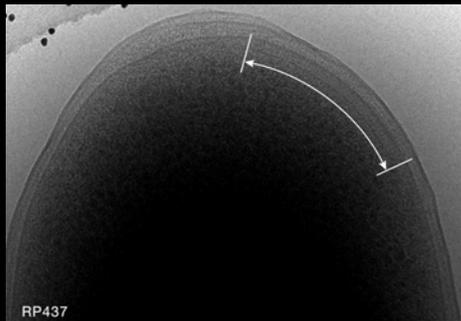
Generation of serial vitreous sections at -150°C



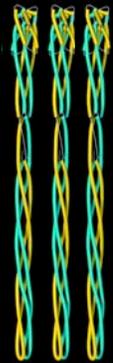
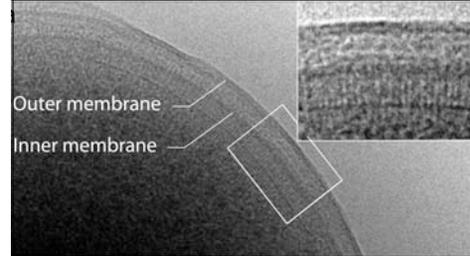
Low-dose images of 20 nm vitreous sections



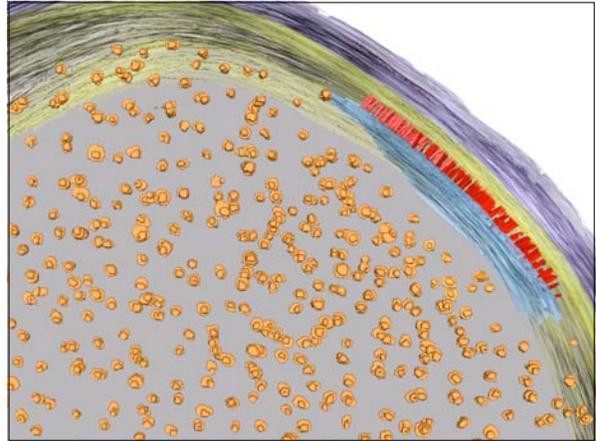
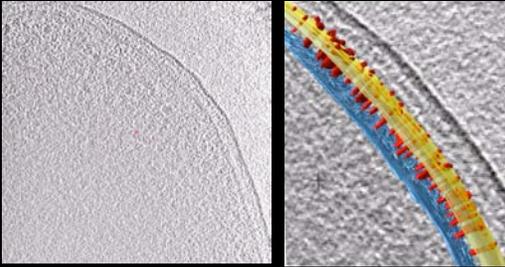
Direct visualization of chemotaxis receptor assemblies in intact *E. coli* cells



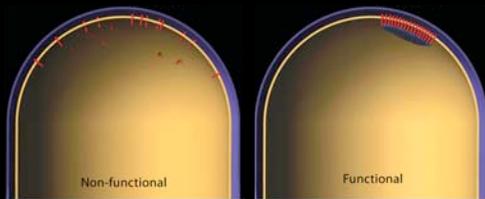
Outer membrane
Inner membrane



Cryo electron tomography of wild-type *E.coli* cells

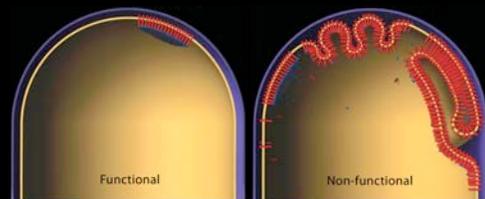


Correlation of expression levels, spatial architecture and physiology



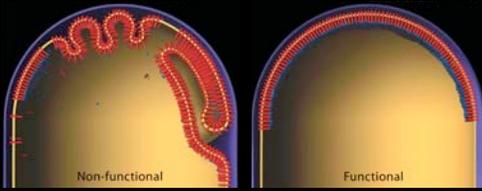
Tsr	+	Tsr	+
CheA/CheW	-	CheA/CheW	+

Correlation of expression levels, spatial architecture and physiology



Tsr	+	Tsr	++
CheA/CheW	+	CheA/CheW	+

**Correlation of expression levels,
spatial architecture and physiology**

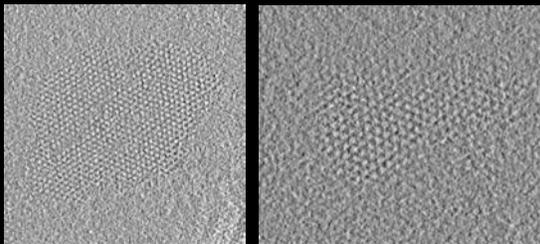


Tsr	++	Tsr	++
CheA/CheW	+	CheA/CheW	++

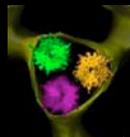
Receptor clusters in cells overproducing Tsr



Receptor clusters in cells overproducing Tsr



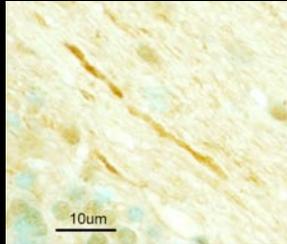
Repeating unit is a trimer of receptor dimers



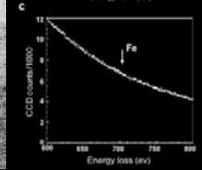
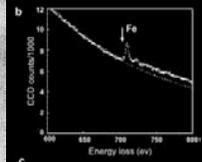
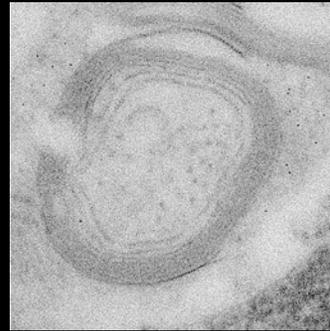
Ferritin localization in degenerating neurons



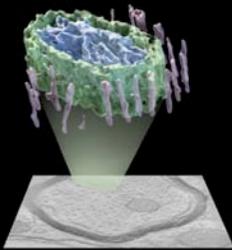
(Tracey Roualt and colleagues at NICHD/NIH)



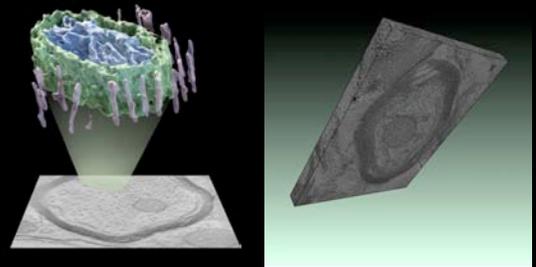
Detection of ferritin in axonal sections



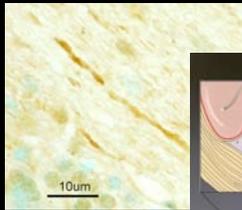
Localization of ferritin in degenerating neurons



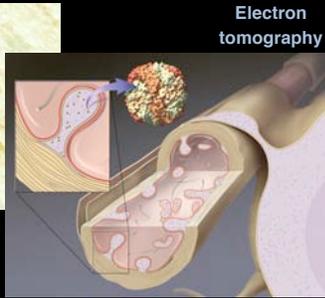
Localization of ferritin in degenerating neurons



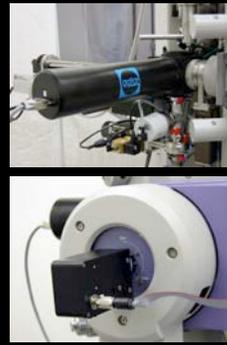
An unexpected discovery!



Conventional optical microscopy



Gatling multi-specimen holder (collaboration with Gatan Inc., UK)



Gatling multi-specimen holder (collaboration with Gatan Inc., UK)



Gatling multi-specimen holder



