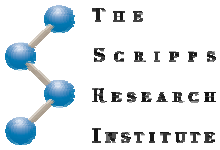


Situs Design, History, Future

Willy Wriggers, Ph.D.
Department of Molecular Biology
The Scripps Research Institute
10550 N. Torrey Pines Road, Mail TPC6
La Jolla, California, 92037

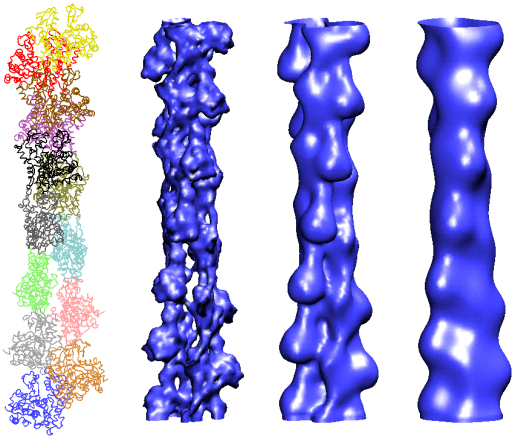
Situs Modeling Workshop, San Diego, CA, Feb. 3-5, 2003

Combining Multi-Resolution Biophys. Data

Actin filament model (Holmes et al., 1990)

Convolution with Gaussian:

$$G(r) = \exp\left(\frac{-3r^2}{2\sigma^2}\right)$$



2σ=0Å 2σ=10Å 2σ=20Å 2σ=40Å

Q: We can lower the resolution of 3D data, but how can one increase it?
A: Combine low- with high-resolution data by flexible and rigid-body fitting.

1998: Vector Quantization

Encode data (in $\Re^{d=3}$) using a finite set $\{w_j\}$ (j=1,…,k) of *codebook vectors*.
Delaunay triangulation divides $\Re^3$ into k *Voronoi polyhedra* ("receptive fields"):

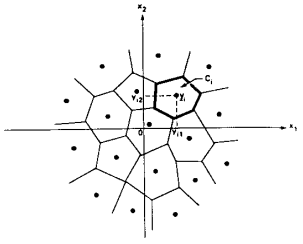
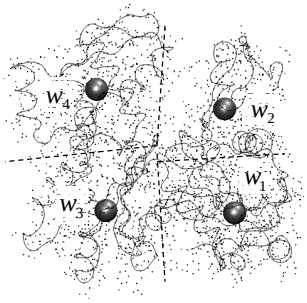


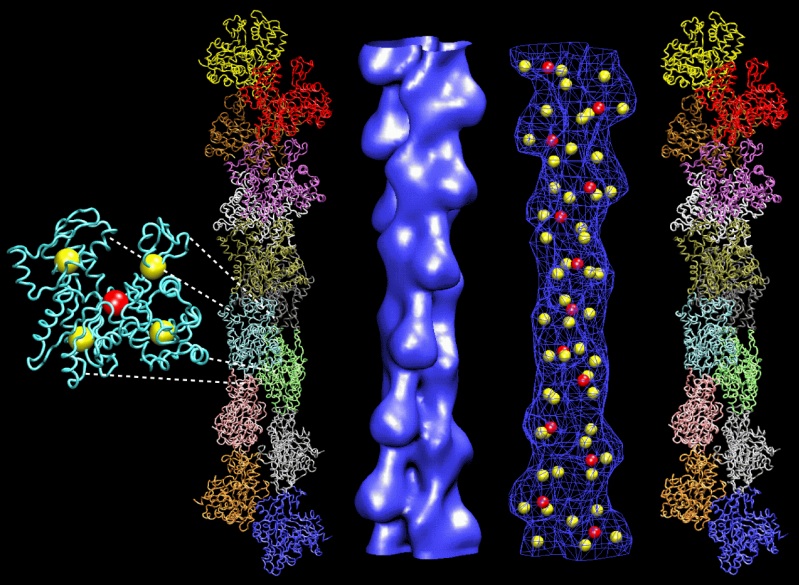
Fig. 3. Partitioning of two-dimensional space ($N = 2$) into $L = 18$ cells. All input vectors in cell C_i will be quantized as the code vector y_i. The shapes of the various cells can be very different.



Encoding Distortion Error: $$E = \sum_{\substack{i \text{ (atoms,} \\ \text{voxels)}}} \left\| v_i - w_{j(i)} \right\|^2 m_i$$

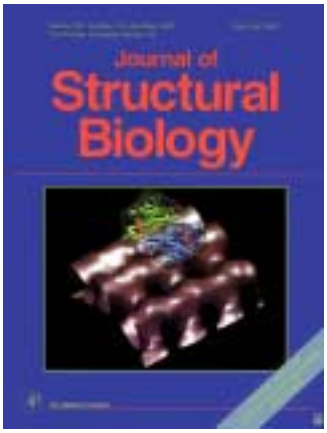
Linde, Buzo, & Gray (1980): Gradient descent finds nearest local minimum of E.
Martinetz & Schulten (1993): Global search with topology-representing neural nets.

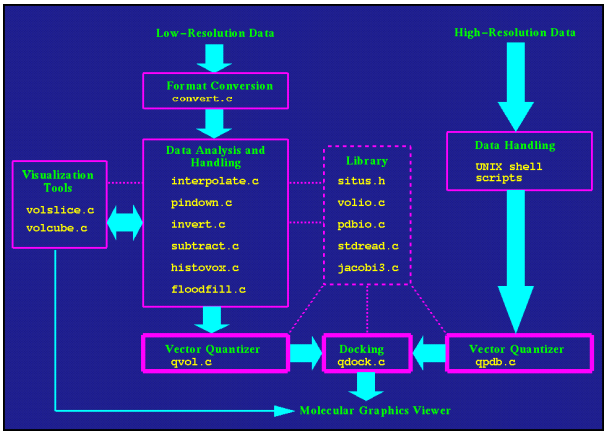
1998:Test on EM Data



Actin filament: Reconstruction from EM data at 20Å resolution rmsd: 1.1Å

1999: Situs 1.0





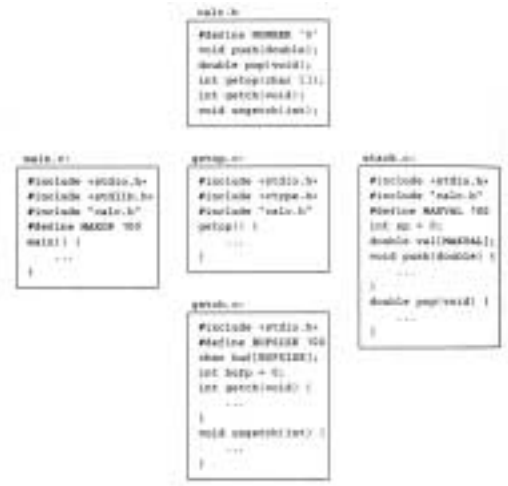
Willy Wriggers, Ronald A. Milligan, and J. Andrew McCammon. Situs: A Package for Docking Crystal Structures into Low-Resolution Maps from Electron Microscopy. *J. Structural Biology*, 1999, Vol. 125, pp. 185-195.

General ANSI C Program Design

Kernigan & Ritchie (1978)

Modular Programming

Header Files .h
Main Programs .c
Library Programs .c



1999: Announcement on the Internet

News groups:

comp.ai.neural-nets
bionet.molec-model
bionet.info-theory
bionet.software
bionet.xtallography
bionet.announce
bionet.biology-computational
bionet.biophysics
bionet.molbio.proteins

Mailing lists:

Computational Chemistry
VMD User List
3D Electron Microscopy

First week

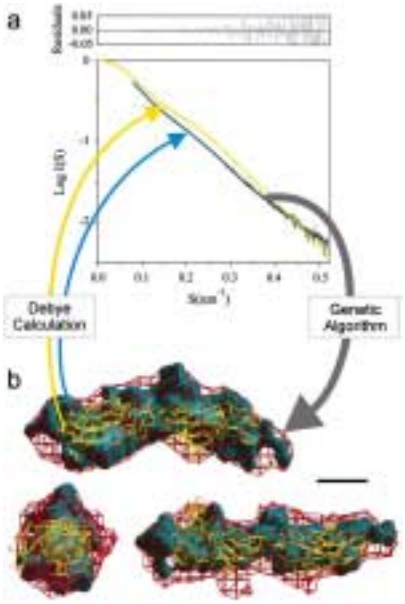
- 20 registered users
- 50 downloads

Today

- 450 registered users
- 2000 downloads

Situs 1.3: Application to SAXS Data

Low-resolution
3D shapes from
1D scattering profiles!

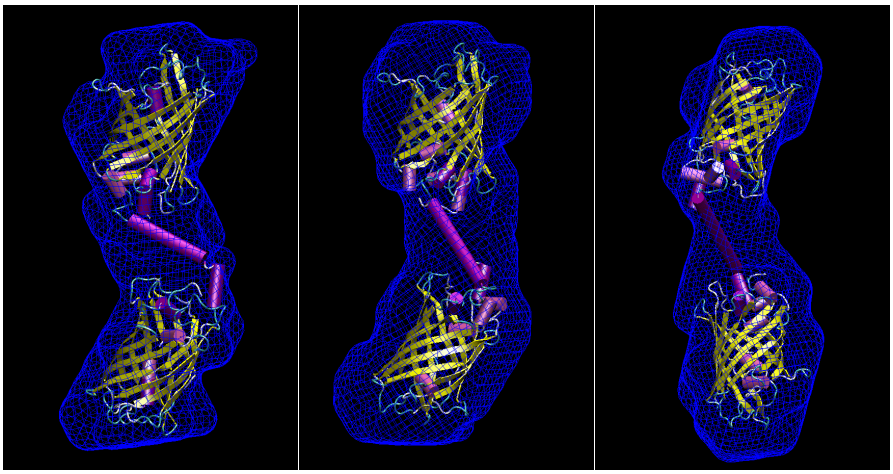


Chacón et al., JMB (2000) 299:1289

SPring-8

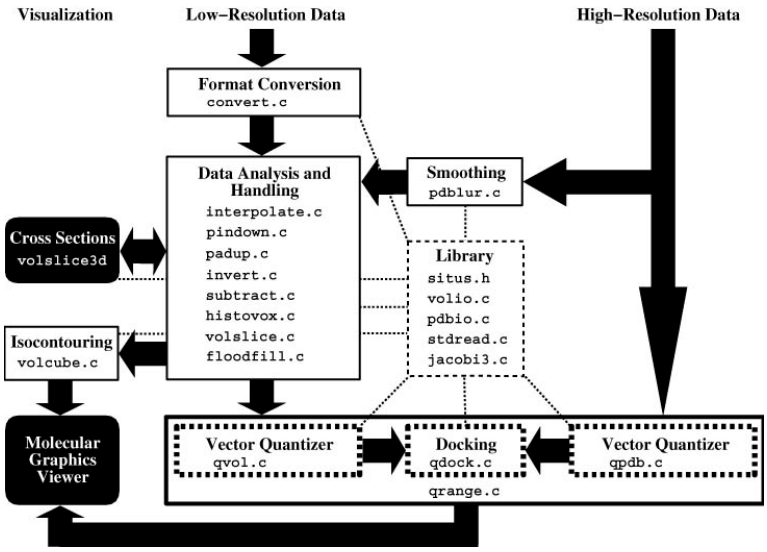
BL45 SAXS Station

EBFP-linker-EGFP fusion proteins
(Tetsuro Fujisawa)

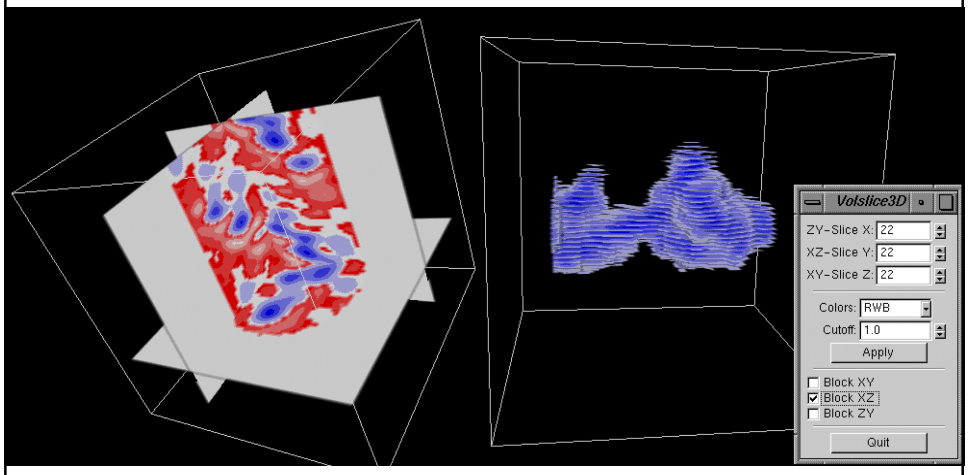


LAEAAAKEAAAKEAAAKAAA (20) LAEAAAKEAAAKEAAAKEAAAKAAA (25) LAEAAAKEAAAKEAAAKEAAAKEAAAKAAA (30)

2001: Situs 1.4



Towards a GUI: *volslice3D*



- OpenGL graphics library developed by Stefan Birmanns, NIC, Jülich, Germany
- support of slicing, isocontouring, 3D textures, stereo, VR devices
- portable to standard UNIX architectures, PC/Linux, and Windows

2001: The CSB Group

Computational
Structural
Biology

CSB Group Members:

Pablo Chacón, TSRI
Essam Metwally, TSRI
Julio Kovacs, TSRI
Yao Cong, TSRI
Stefan Birmanns, Jülich, Germany

TSRI Collaborators:

Ron Milligan, TSRI
Florence Tama and Charlie Brooks, TSRI

Funding:
NIH, Burroughs Wellcome Fund

situs.scripps.edu
VERSION 2.0

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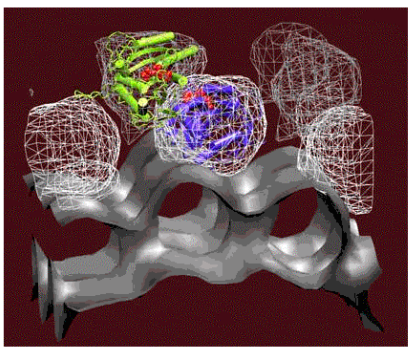
User Guide
Tutorials
Methodology
References
History
Upcoming Events:
Biophysical Discussions, April 19-22
EM Symposium, ACA2002, May 25-30
Electron Cryst. School, Tampere, Finland, June 7-12
Other Sites of Interest:
Volslice3D
VMD
EM Info | Online Course
SAXS Info
CSB Group

Integrating structural data from a variety of biophysical sources...



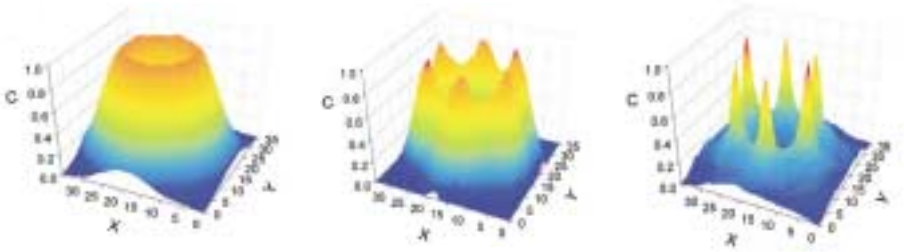
Situs is an award-winning program package for the modeling of atomic resolution structures into low-resolution density maps e.g. from electron microscopy or small angle X-ray scattering . The software supports both rigid-body and flexible docking using a variety of fitting strategies. Situs is developed by the Computational Structural Biology group at The Scripps Research Institute .

Fast Matching and Filtering

Resolution 15 Å
Grid size 4Å
ΔAngle 9º

Fast Translational Matching:
CoLoRes (P. Chacón)
Fast Rotational Matching (J. Kovacs)

No filter **Local mask** **Laplacian filter**



Increasing Fitting Contrast →

The Scripps Research Institute, La Jolla, CA

University of Texas-Houston
(Texas Medical Center)

Virtual Reality: *SenSitus*

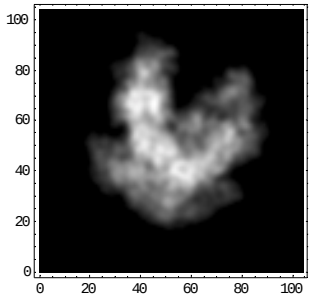
School of Health Informatics, University of Texas-Houston

PHANTOM™ 1.5/6DOF
Haptic Device:
Force-Feedback in 6 DOF

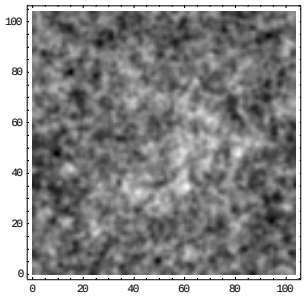
Testing a Prototype of ***SenSitus***
in an immersive VR environment:
Holobench (S. Birmanns).

2D Image Processing with Fast Rotational Matching

Yao Cong, in collab. with S. Ludtke (EMAN)
and P. Penczek (SPIDER)



(a) Reference image (after applying a Gaussian low-pass filter with half-width 1/10 $Å^{-1}$)



(b) Particle image, (a) corrupted by Gaussian noise scale=0.26

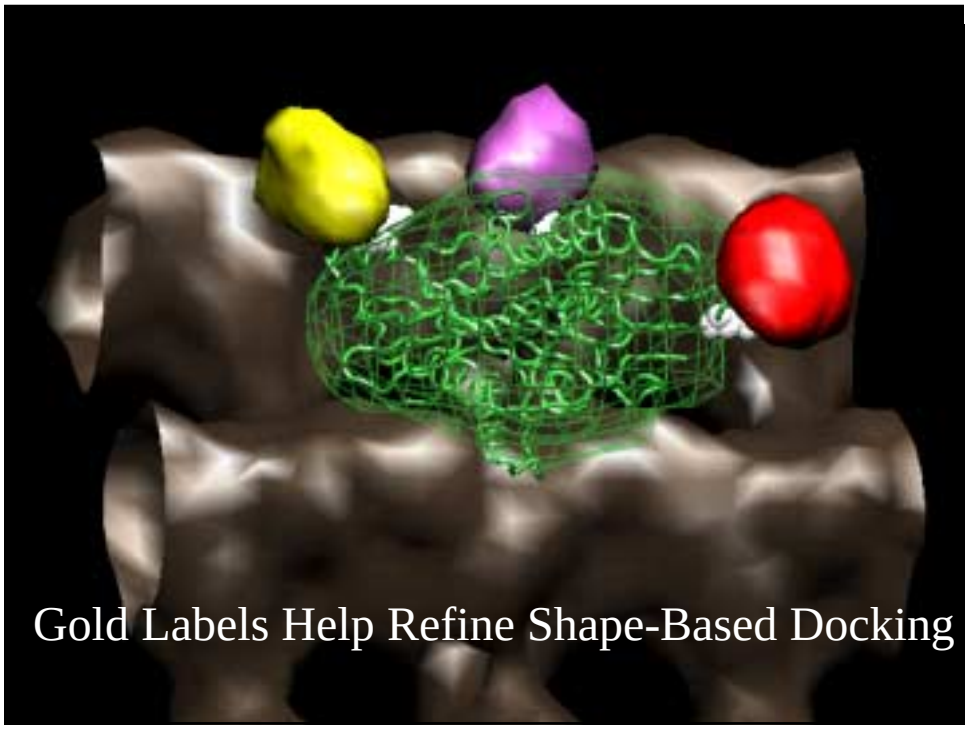
Electron Microscopy

THE UNIVERSITY of TEXAS
HEALTH SCIENCE CENTER at HOUSTON
INSTITUTE of MOLECULAR MEDICINE
for the PREVENTION of HUMAN DISEASES

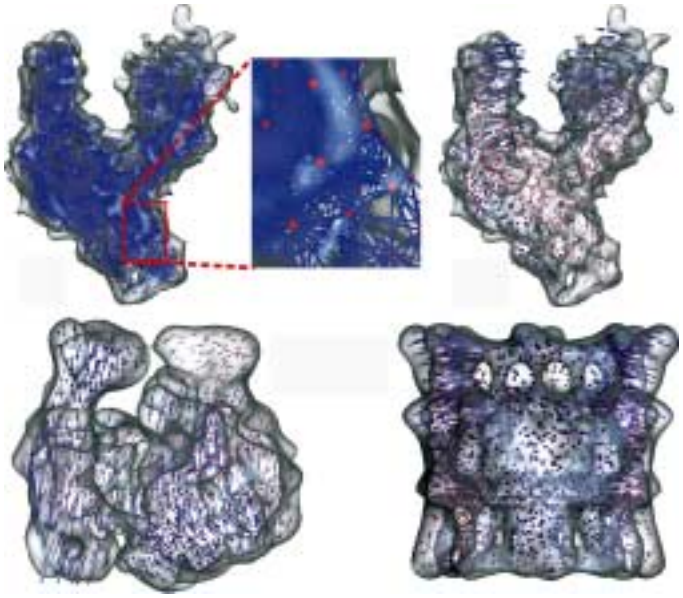
Leo (Zeiss) 912

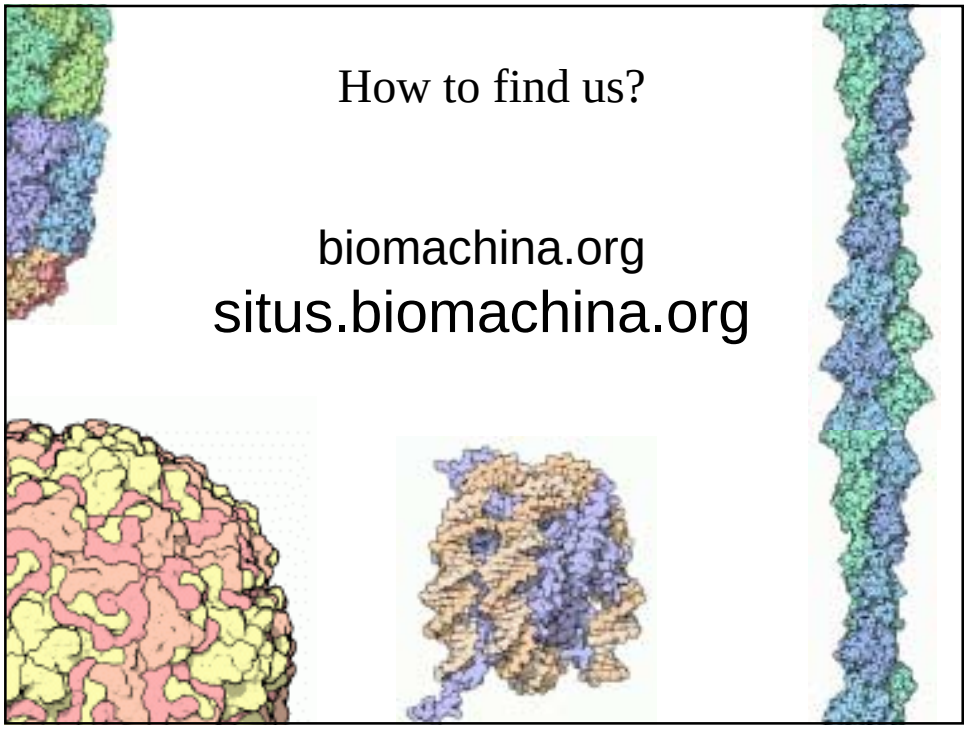
- **Resolution:** 0.37nm
- **Voltage:** 60 to 120kV
- **Magnification:** 80 - 500,000x

Inquire about postdoctoral openings!



Normal Mode Analysis

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