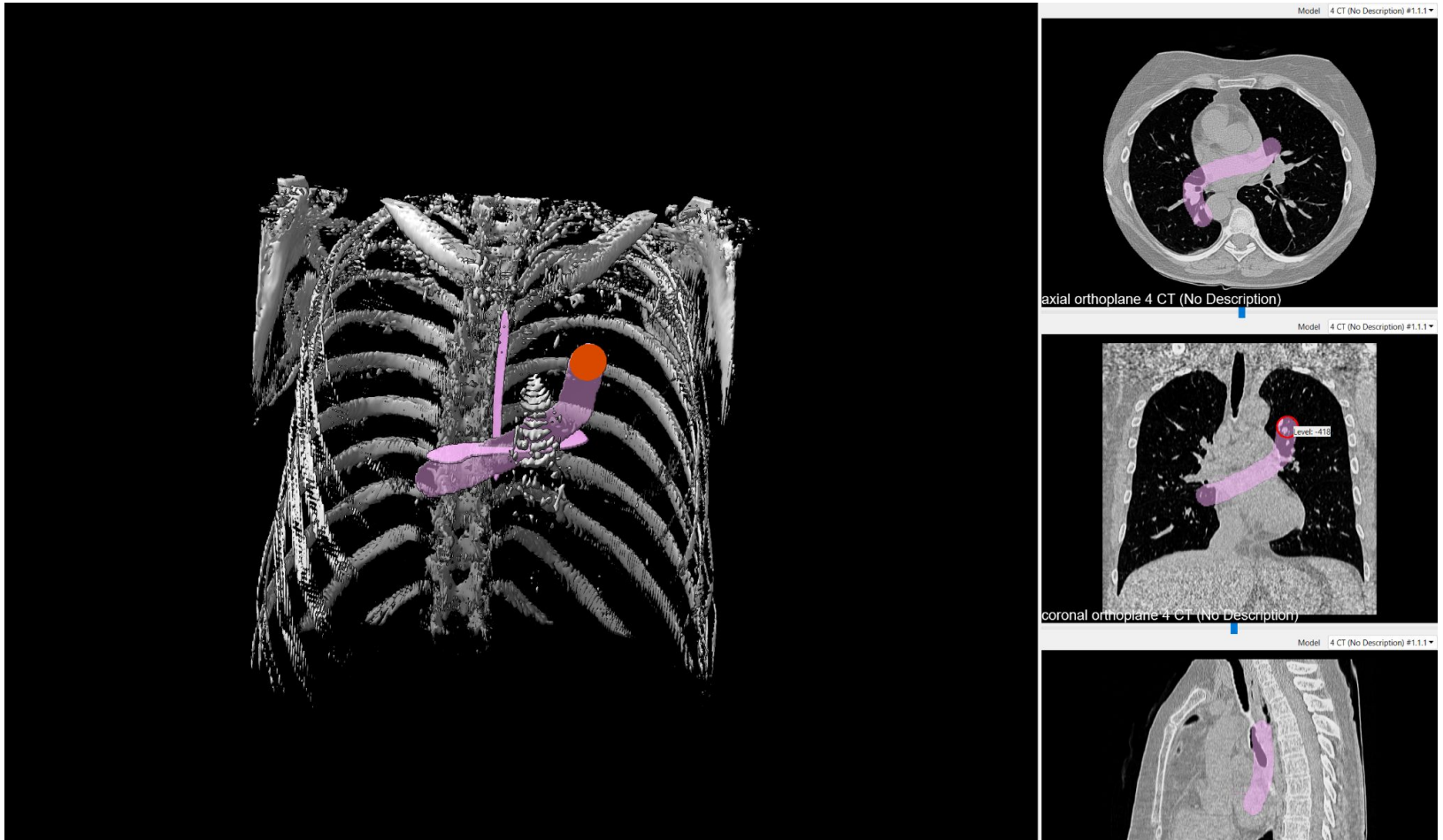
UCSF ChimeraX for Cryo-EM

University of Kansas
9 November 2023

Background


Thu, Feb, 09, 2023
Campus content
EDUCATION INTERVIEW DAY
Touch for building directory
KU


Model
4 CT (No Description) #1.1.1
axial orthoplane 4 CT (No Description)
Model
4 CT (No Description) #1.1.1
Level: -418
coronal orthoplane 4 CT (No Description)
Model
4 CT (No Description) #1.1.1

Brief History of the RBVI

- 1969: Robert Langridge establishes the Computer Graphics Lab at Princeton University
- 1976: CGL moves from Princeton to UCSF
- 1978: Molecular Interactive Display System (MIDS)
- 1988: Simulation added to MIDS, MIDS becomes MIDAS
- 1993: Tom Ferrin becomes the PI of the CGL's "P41" NIH grant
- 1994: Langridge retires
- 2000: CGL renamed to Resource for Biocomputing, Visualization, and Informatics
- 2002: UCSF Chimera released
- 2017: UCSF ChimeraX alpha release
- 2020: UCSF ChimeraX gets a 1.0 release

But enough about that...

Let’s look at some Cryo-EM data

https://www.rbvi.ucsf.edu/chimerax/data/stanford-apr2022/cryoem_intro.html

Introduction to ChimeraX for cryoEM Atomic Structures

Tom Goddard
April 25, 2022
for Wah Chiu's Stanford cryoEM class

Introduction to using ChimeraX to analyze cryoEM maps and atomic models. We will look at recent mouse insulin receptor structures published March 31, 2022, map EMDB 25428 and atomic model PDB 7STH.

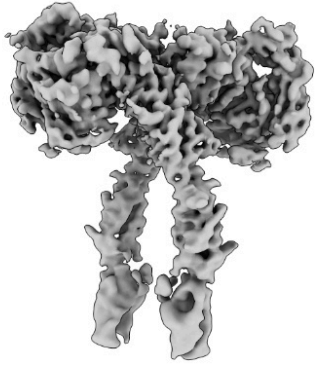
> Synergistic activation of the insulin receptor via two distinct sites
> Jie Li, Junhee Park, John P. Mayer, Kristofor J. Webb, Emiko Uchikawa, Jiayi Wu, Shun Liu, Xuewu Zhang, Michael H. B. Stowell, Eunhee Choi & Xiaochen Bai
> Nature Structural & Molecular Biology volume 29, pages 357-368 (2022)

Topics

- How to look at cryoEM map contour surfaces.
- Working with atomic models.
- Using AlphaFold Database atomic models.
- Fitting atomic models in maps.
- Morphing between atomic models to view conformational changes.

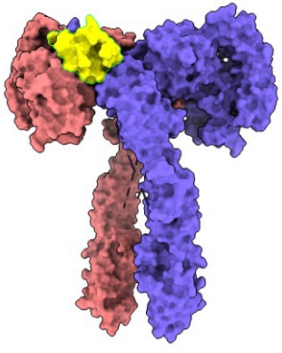
How to look at cryoEM map contour surfaces

1. Look at EMDB 25428, 3.5A resolution, 60 MB file size.
   Command: open 25428 from emdb
2. Adjust threshold with histogram slider or command
   volume #1 level .03
3. Adjust step size to show full resolution.
   volume #1 step 1
4. Use soft lighting from toolbar for shadows.
   light soft
5. Save image with toolbar **snapshot** button.
   save irmap.png



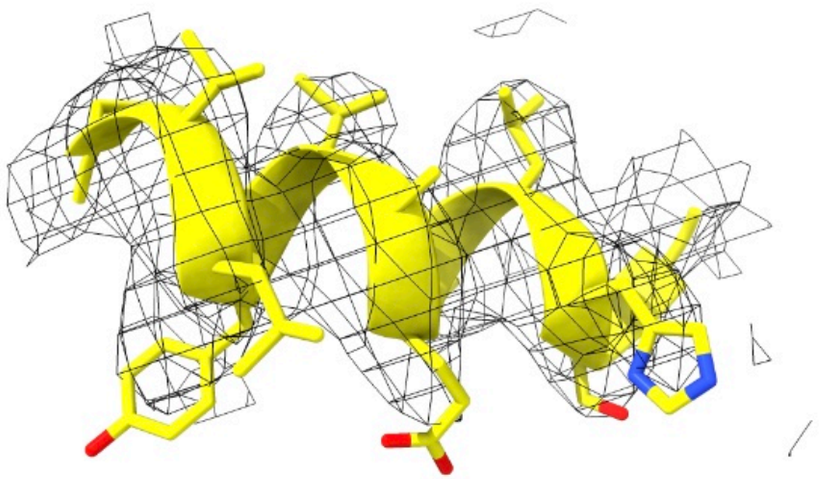
Working with atomic models

6. Open atomic model that was built into map
   open 7sth
7. Undisplay map with **Models panel** or command
   hide #1 model
8. Color by chain with **Molecule Display toolbar** or
   color #2 bychain
9. Show surfaces with **Molecule Display toolbar** or
   surface #2
10. Select insulin chain D with link in log or
    select /D
11. Color insulin yellow with menu **Actions / Color / yellow** or
    color sel yellow



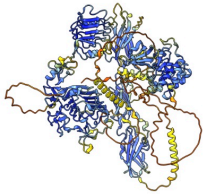
Show map quality near atomic model

12. Look at map near one helix of insulin.
13. Clear selection with menu **Select clear**
    select clear
14. Hide surfaces with Molecule Display toolbar.
    hide #2 surface
15. Select one insulin helix with ctrl-click on ribbon followed by up arrow key
    select /D:8-19
16. Hide ribbon except for selected helix
    hide ~sel ribbon
17. Show map with Models panel
    show #1 model
18. Use menu **Tools / Volume Data / Surface Zone** near **selected atoms**
    volume zone #1 near sel range 3
19. Change map style to **Mesh** in **Volume Viewer panel**
    volume #1 style mesh
20. Show atoms of helix with menu **Actions / Atoms / show**
    show sel
21. Color nitrogens blue, oxygens red with Molecule Display toolbar color **heteroatom**
    color sel byhet

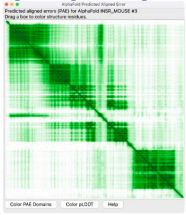


Using AlphaFold Database atomic models

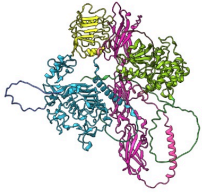
22. Use an AlphaFold model to start building an atomic model from the map.
23. Fetch AlphaFold prediction for UniProt INSR_MOUSE using menu **Tools / Structure Prediction / AlphaFold**.
    alphafold match INSR_MOUSE



24. AlphaFold per-residue confidence coloring: high blue, low red.
25. Show AlphaFold predicted aligned error (PAE) plot with AlphaFold panel **Error Plot** button.
    alphafold pae #3 uniprot INSR_MOUSE



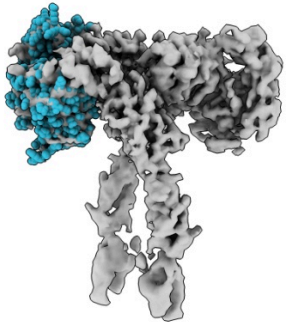
26. Color PAE domains using button on PAE plot. AlphaFold is not confident of the packing of different colored domains.
    alphafold pae #3 colorDomains true



27. Blue, yellow and pink domains are extracellular and in map. Green is cytoplasmic kinase not in map.

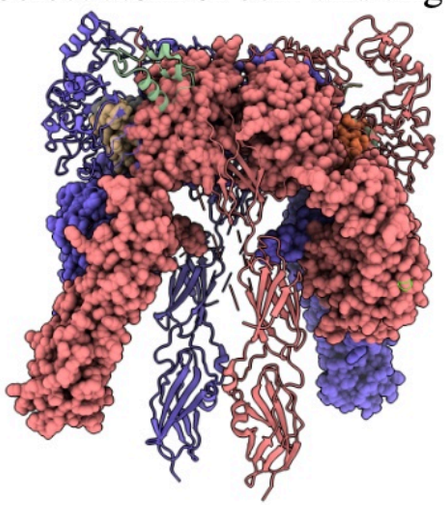
Fitting atomic models in maps

28. Fit blue AlphaFold domain in map.
29. Delete residues outside blue domains 28-336.
    delete #3:1-27,337-end
30. Redisplay full map as surface.
    volume unzone ; volume style surface
31. Move blue domain into map with **Move Model** mouse mode from **Right Mouse toolbar**.
    ui mousemode right "translate selected models"
32. Ctrl click blue ribbon to select it.
    select #3
33. Move blue domain into map with right mouse (on Mac Option key + trackpad drag). Hold Shift key to rotate.
34. Use **Fit** button on **Map toolbar** to optimize position in map.
    fitmap #3 in #1
35. Show atoms as spheres to see fit better. Clear selection (ctrl-click background) then Molecule Display toolbar show atoms and sphere style.
    select clear ; show #3 ; style #3 sphere

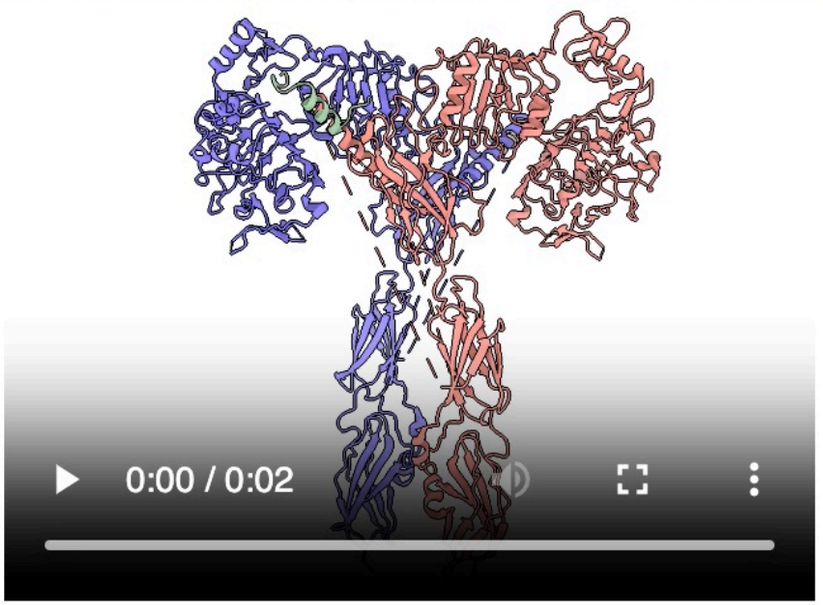


Morphing between atomic models to view conformational changes

36. Above article describes 10 conformations of insulin receptor.
37. Open inactive form of receptor, PDB 7SL1.
    open 7sl1
38. Show 7sth atomic model and hide map and alphafold model.
    show #2 model ; hide #1,3 model ; show #2 ribbon
39. Color by chain using Molecule Display toolbar.
    color bychain
40. Select atom of 7sl1 and align it by hand with move model mouse mode.



41. Calculate morph using command
    morph #2,4 same true
42. Reset morph slider to start and press **Record** button (red circle) to record a movie.
    movie record ; coordset #5 ; wait 50 ; movie encode



43. Separation of intracellular kinases inactivates them.