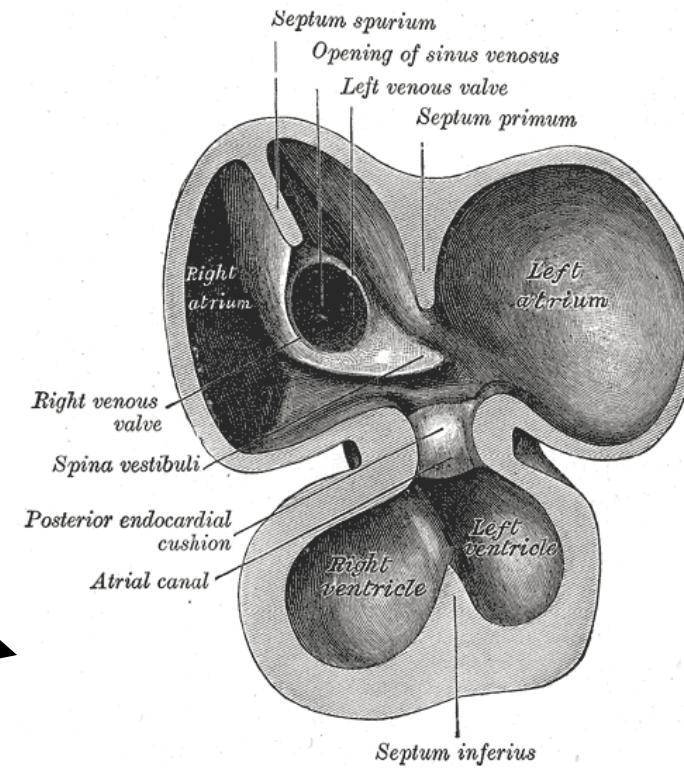
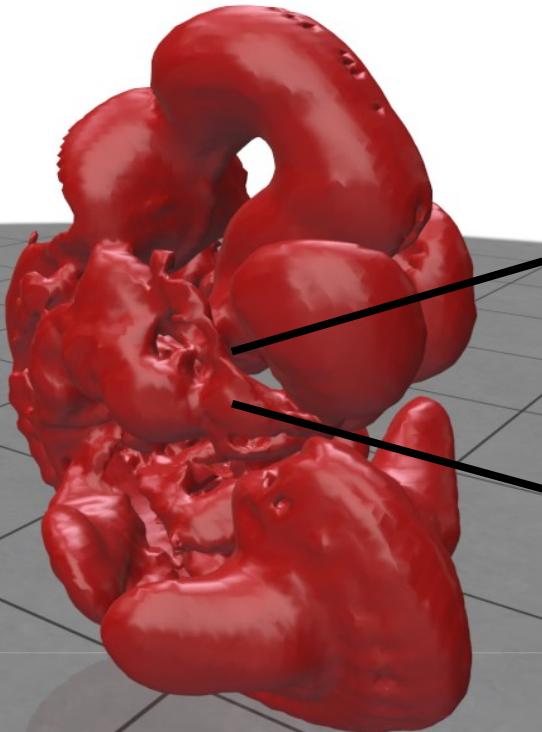




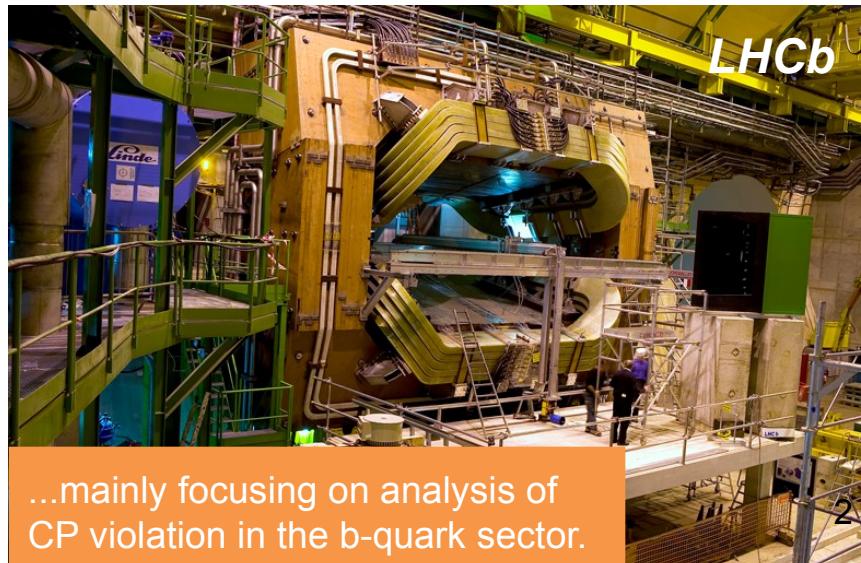
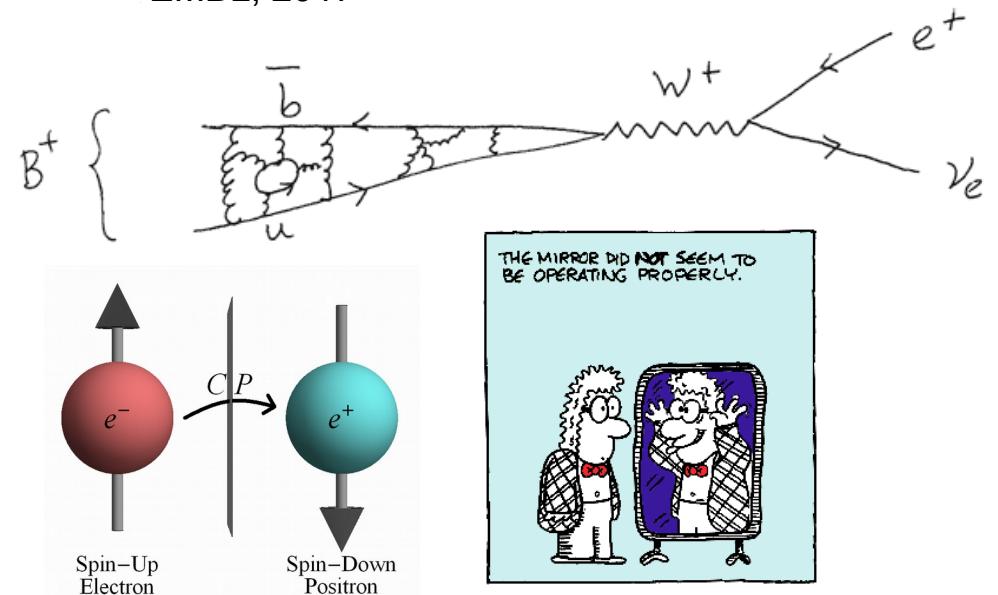
Fearless Hearts



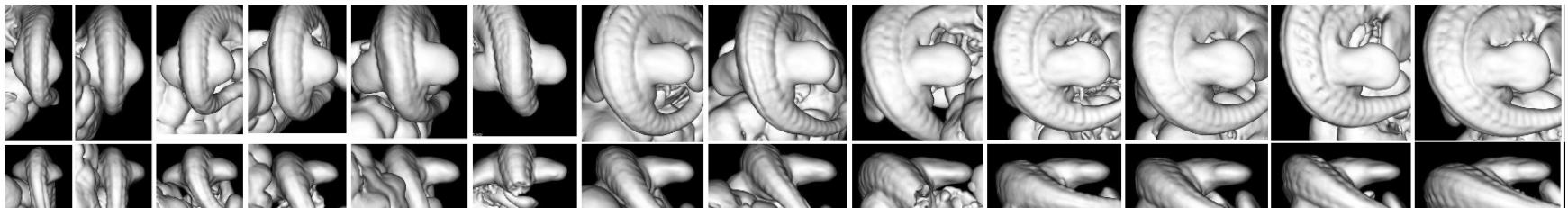
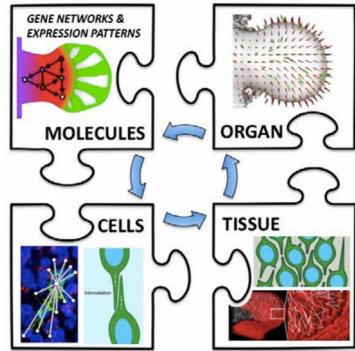
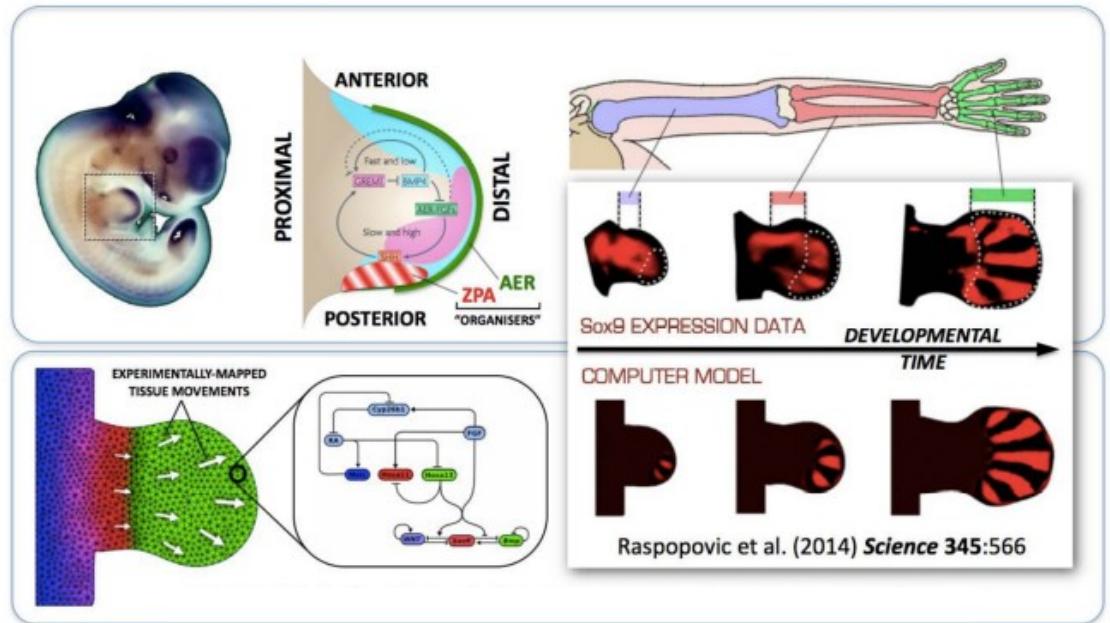
Background

Elementary particle physicist, worked at

- Fermilab (Illinois), 1999
- CERN (Geneva), 2001
 - Physics Dept., Univ. of Milan
 - Physics Dept., UB (Barcelona)
- CRG, 2012
- EMBL, 2017



In Sharpe Lab



OptiHeart Project

- Cardiac organogenesis in mouse models to pinpoint differences between normal and abnormal heart morphology in collaboration with Juanjo Sanz-Esquerro, CNIC (Madrid)
- Two experimental datasets (data collected in 2013):
 - 26 OPT scanned WT embryos using MF-20 as the molecular marker
 - 19 OPT scanned KO embryos with heart defects due to a mutation in the *Arid3b* gene

Goals of this project

Morphometric phenotyping
of subtle mutants

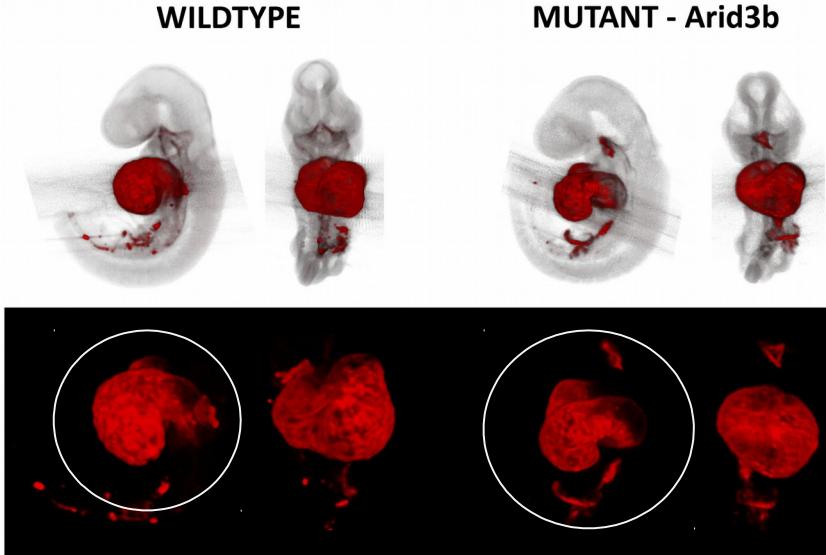
Shape differences between normal and mutant development are not obvious by eye

..becoming more evident only at a later stage

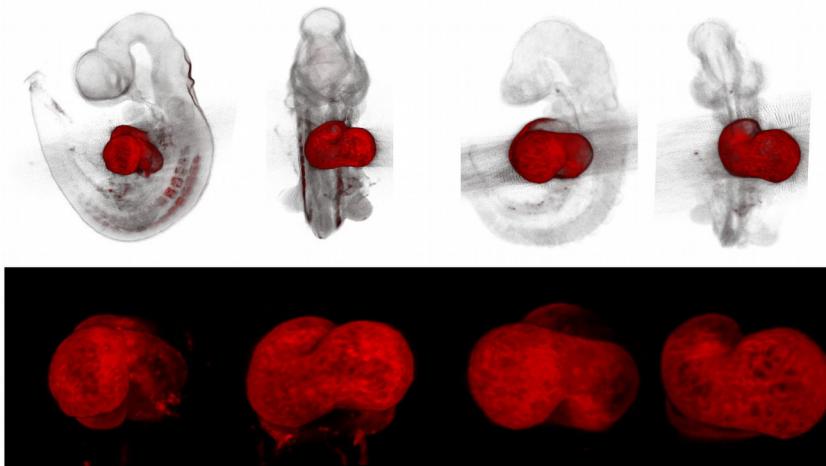
How early can we detect morphological differences?



18 SOMITES



28 SOMITES



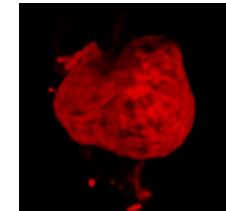
Goals of this project

Create an accurate quantitative 4D model of heart development

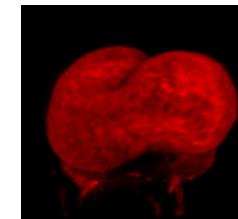
Starting from a discrete set of data points build a continuous description of the morphological development as function of time, both for WT and KO

Can we fill/interpolate the gaps in space and time?

WT



#18
somites

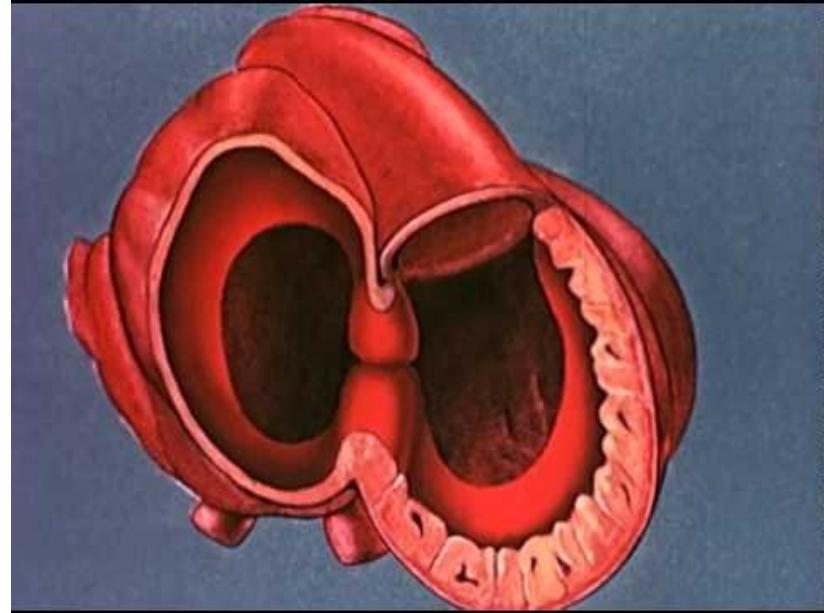


#28
somites

Heart development

The heart develops from two populations of cardiac progenitors (Buckingham et al., 2005)

- Initial heart tube (which will form the left ventricle) originates from cardiogenic mesodermal cells, which fuse at the ventral midline of the embryo.
- Elongation of the heart is driven by the addition at the poles of a second pool of progenitor cells located in the pharyngeal mesoderm beneath the heart tube and called the second heart field (SHF) (Kelly, 2012)



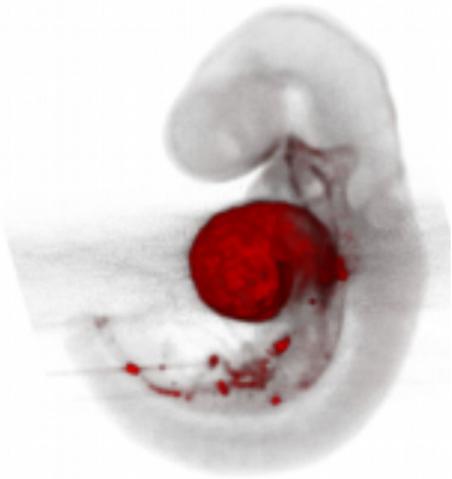
"Normal Development of the Heart"

<https://www.youtube.com/watch?v=5DIUk9IXUai>

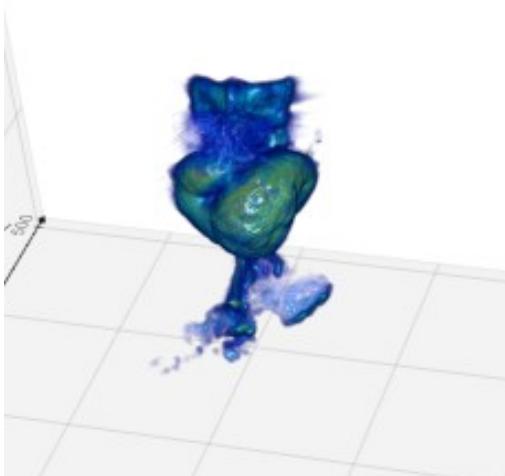
Arid3b, is a member of the conserved ARID family of transcription factors, is essential for mouse embryonic development but its precise roles are poorly understood

- expressed in the myocardium of the tubular heart and in SHF progenitors
- *Arid3b*-deficient embryos show cardiac abnormalities: shortening of the poles, absence of myocardial differentiation and altered patterning of the atrioventricular canal, which also lacks ETM

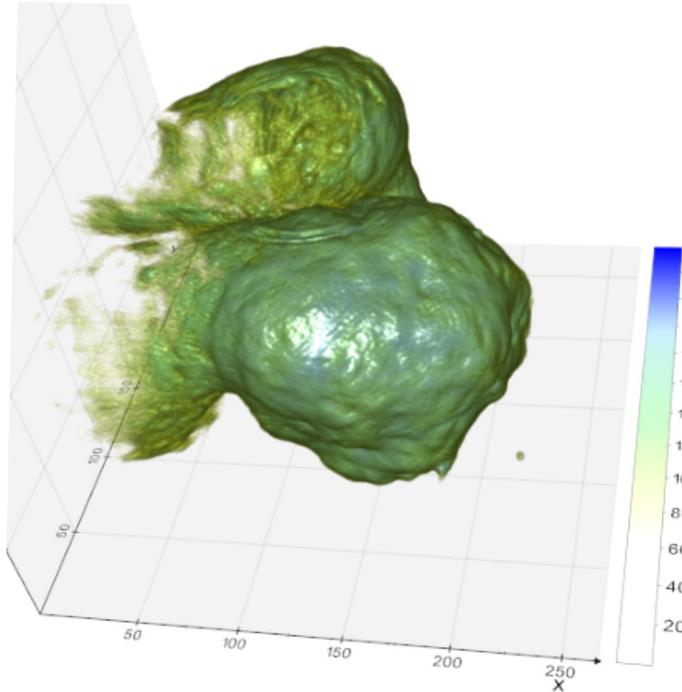
Data massaging



OPT scanned



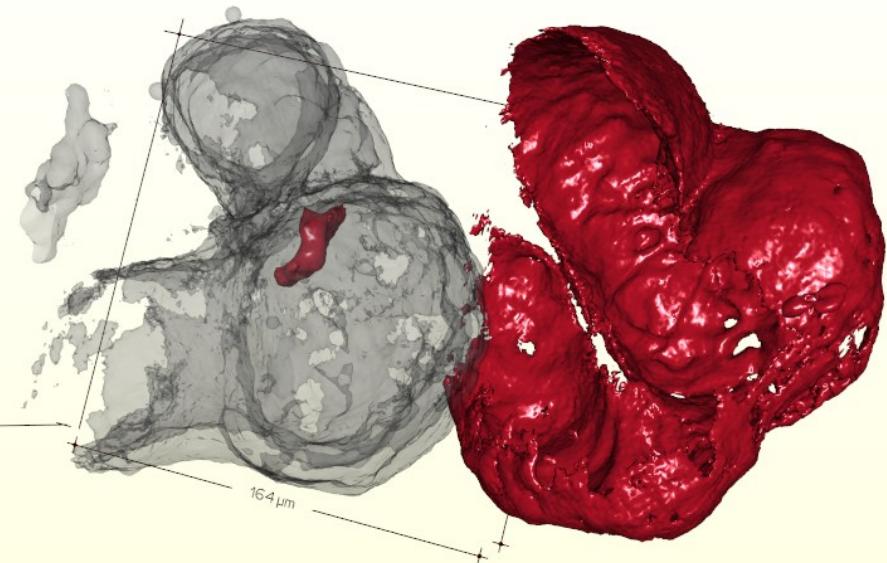
Digitized



Digitized &
cleaned up

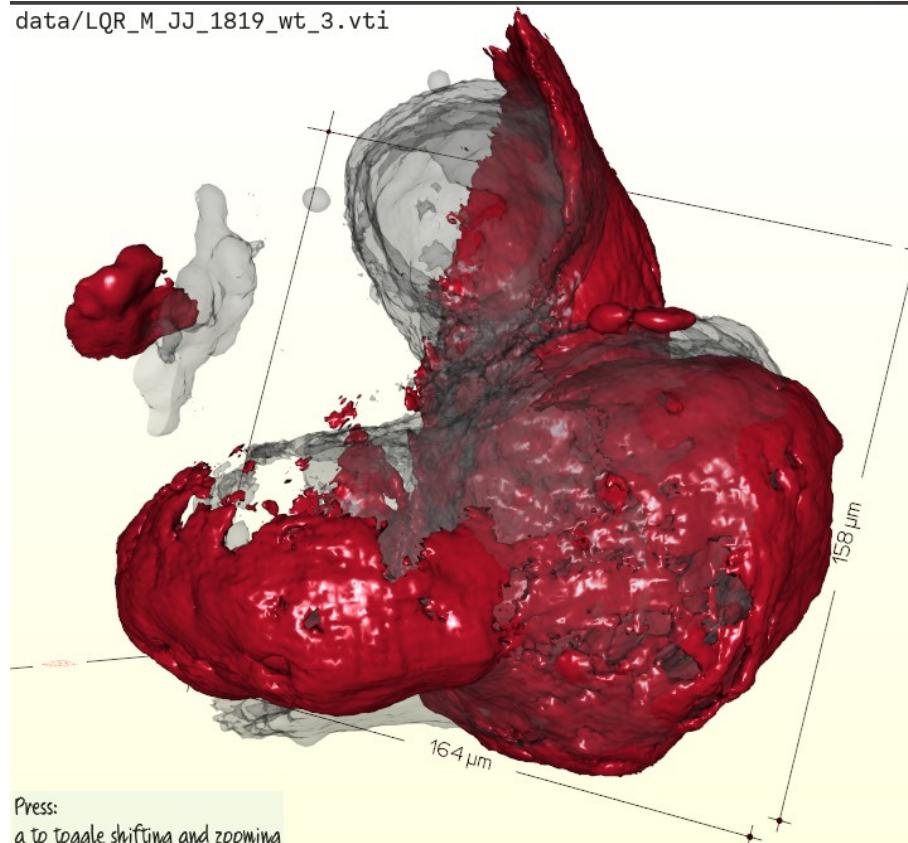
Dataset registration

data/LQR_M_JJ_1819_wt_3.vti

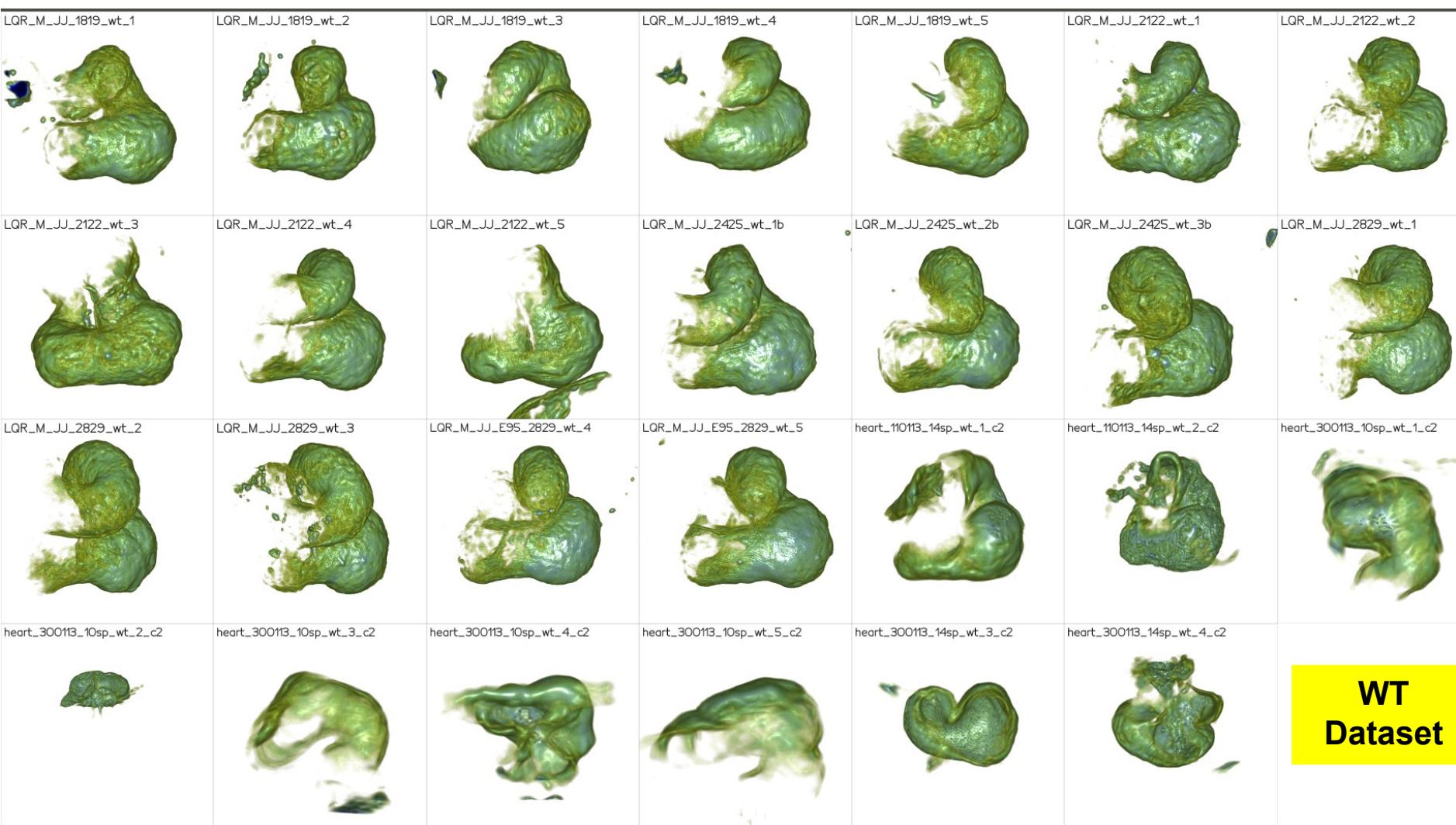


Press:
a to toggle shifting and zooming
q to proceed when happy
F1 to abort session.

data/LQR_M_JJ_1819_wt_3.vti



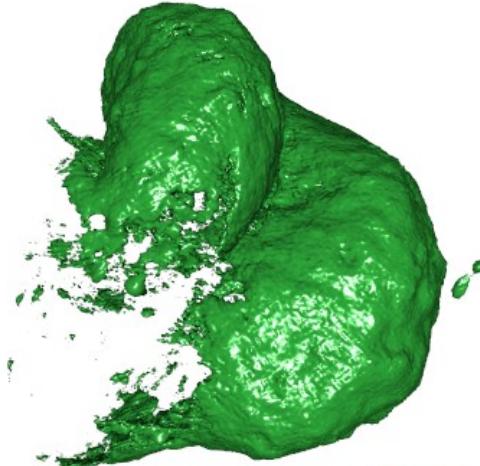
Press:
a to toggle shifting and zooming
q to proceed when happy
F1 to abort session.



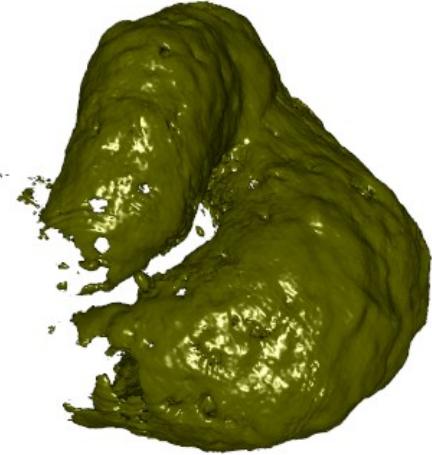
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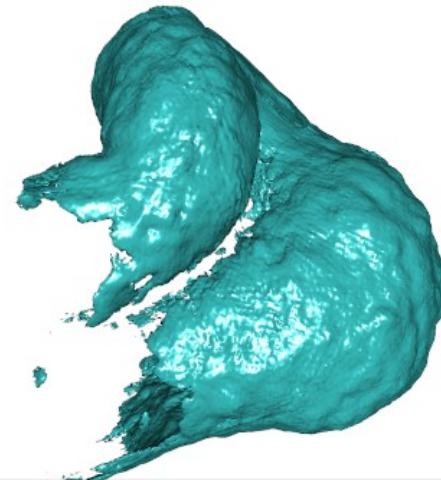
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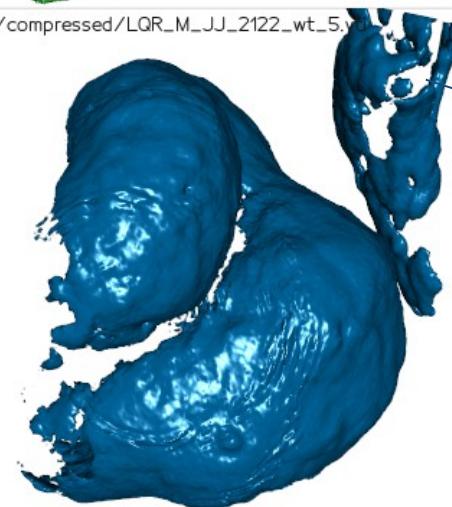
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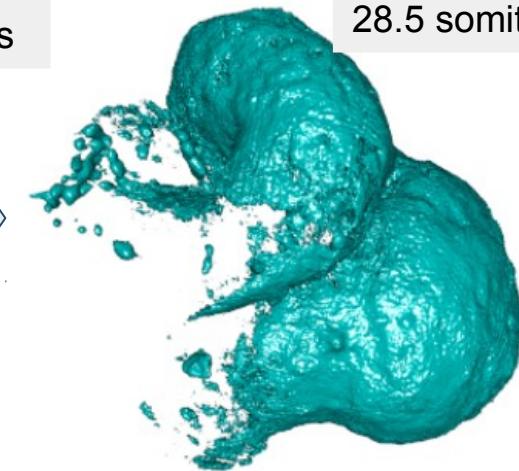
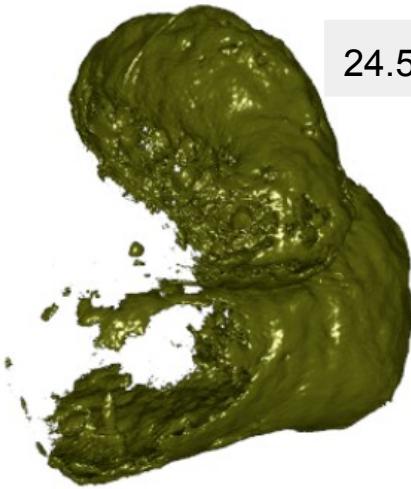
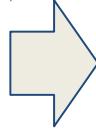
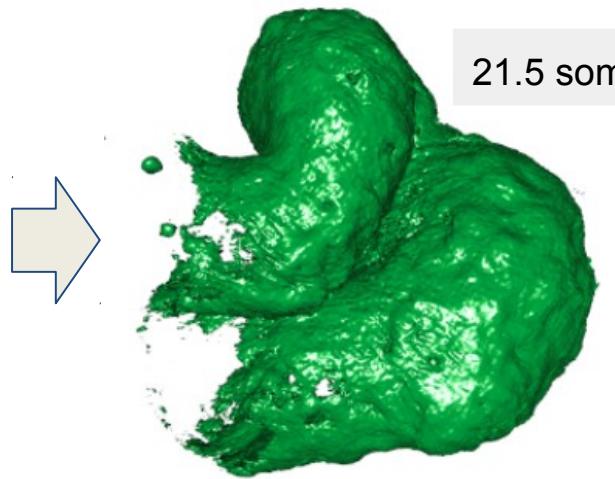
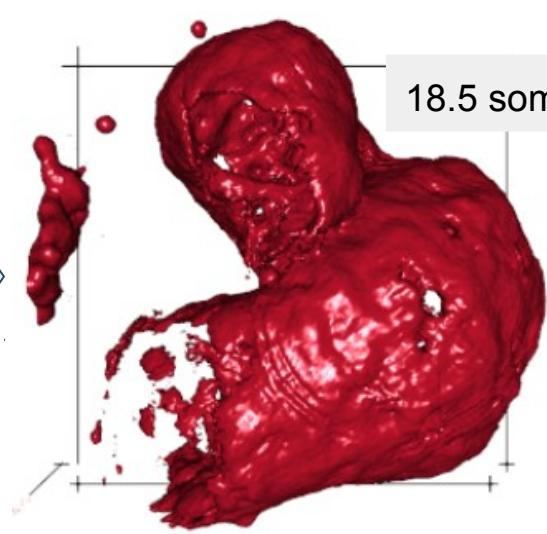
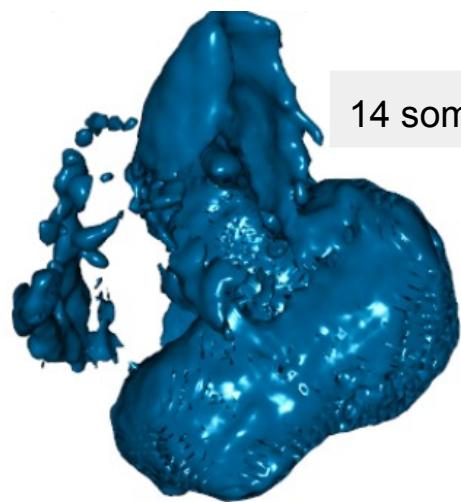
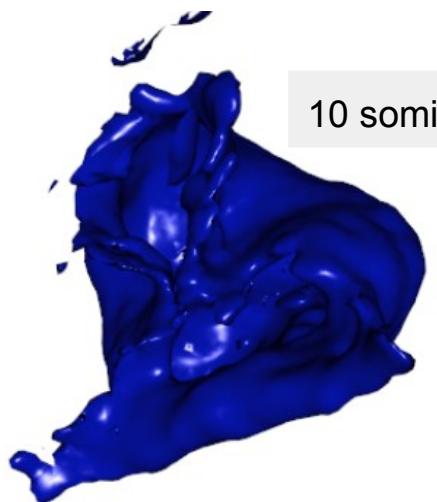
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noise!

stage 21.5

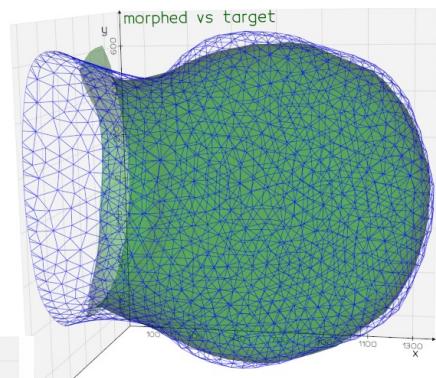
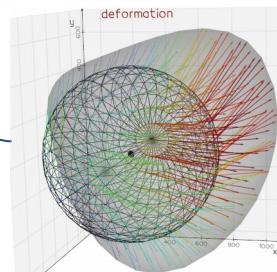
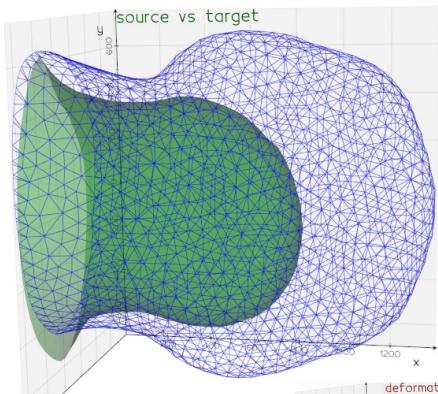
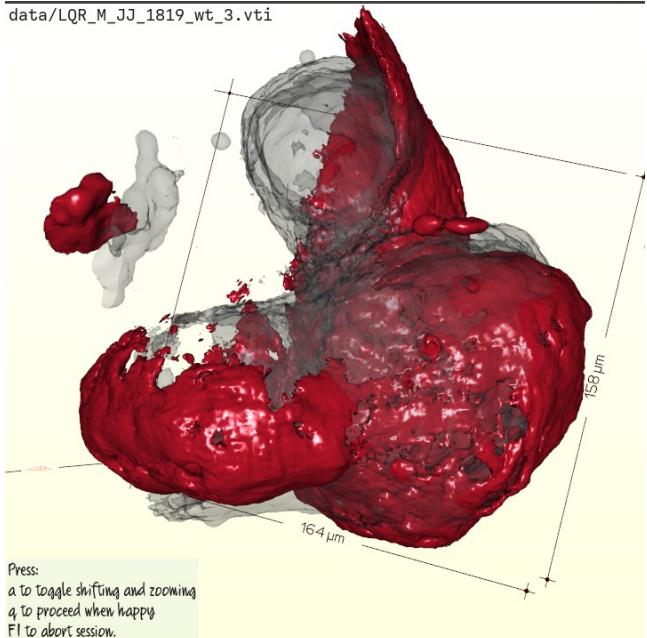
timecourse



Morphing shapes/volumes

squishy/jelly like soft tissue needs more degree of freedom than a rigid registration offers

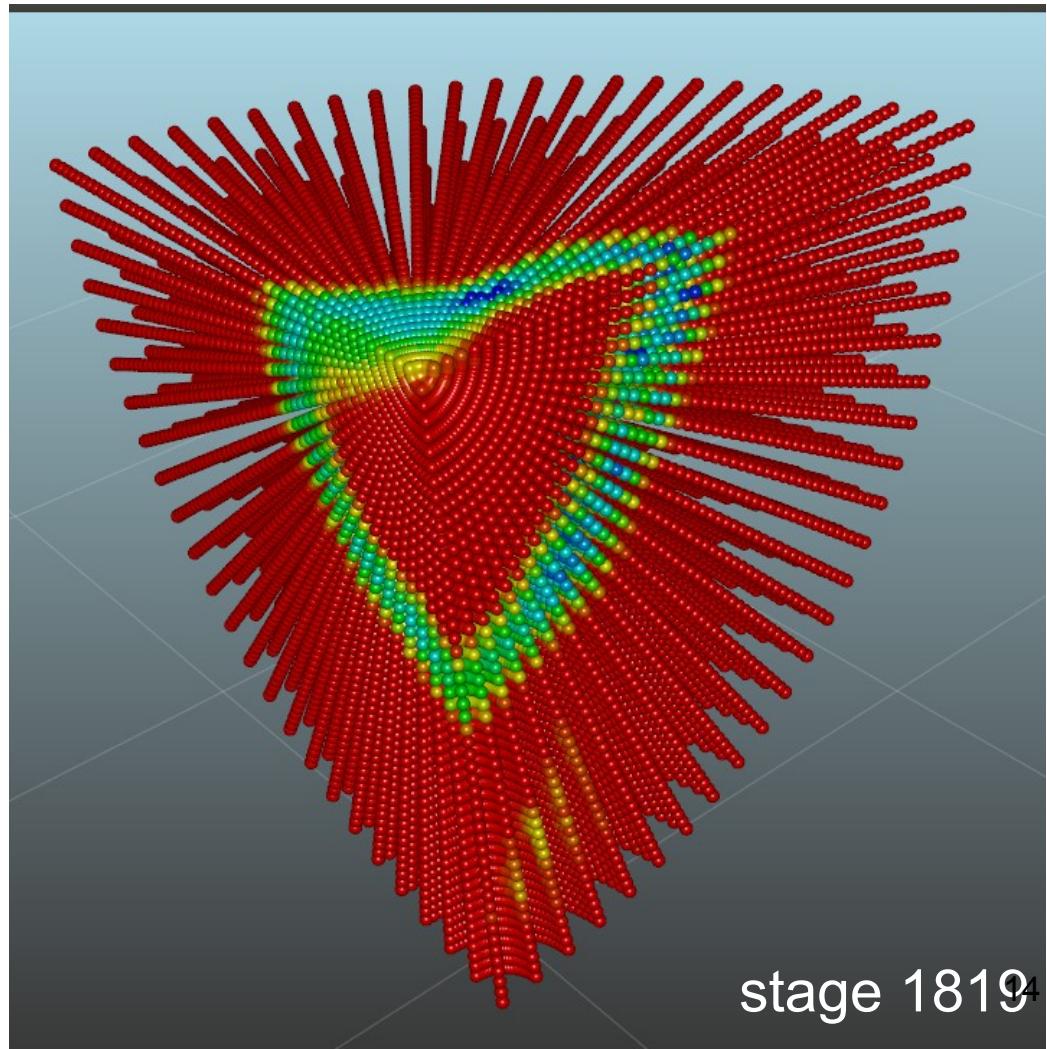
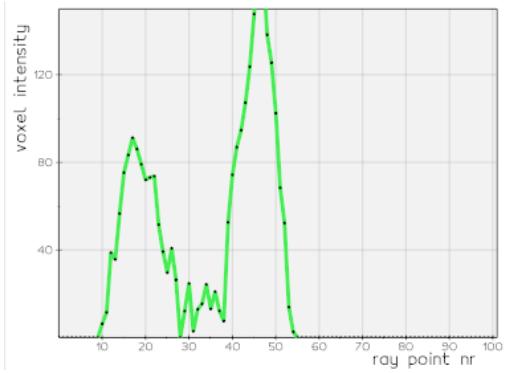
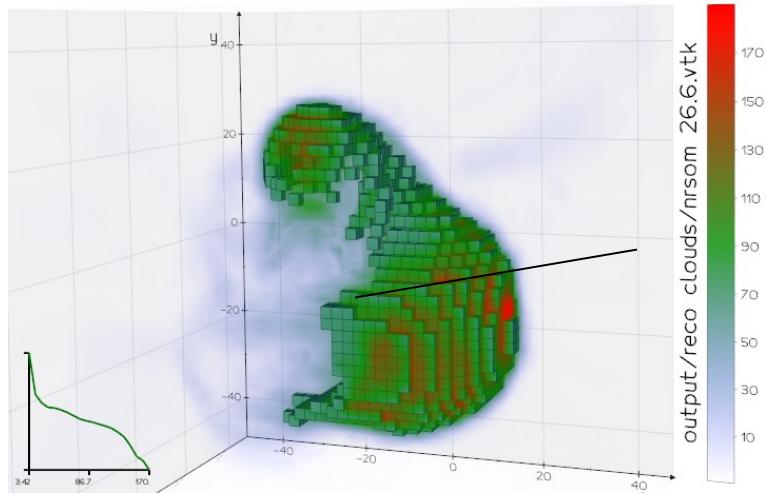
data/LQR_M_JJ_1819_wt_3.vti



Set $\mathbf{T}(x,y,z) = 1 + \delta\mathbf{T}(x,y,z)$
 $\delta\mathbf{T}$ is expanded in Taylor serie and truncated at the first order:
 $\delta\mathbf{T}_{ij}(x,y,z) = a_{ij}(x - x_0) + b_{ij}(y - y_0) + c_{ij}(z - z_0)$
-> 18 free parameters independent of rotations, translations and scaling

..to be tested in the heart case!

Probing voxels with rays



stage 1819

Spherical harmonics demystified

Somehow analogous to **Taylor** expansion:
represent a function near to a point with a set of scalars

$$f(a) + \frac{f'(a)}{1!}(x-a) + \frac{f''(a)}{2!}(x-a)^2 + \frac{f'''(a)}{3!}(x-a)^3 + \dots,$$

..but now in 2 discrete dimensions l and m (with $|m| < l+1$)

$\ell = 0$ [edit]

$$Y_0^0(\theta, \varphi) = \frac{1}{2} \sqrt{\frac{1}{\pi}}$$

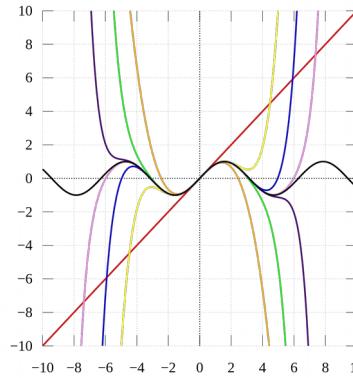
$\ell = 1$ [edit]

$$Y_1^{-1}(\theta, \varphi) =$$

$$\frac{1}{2} \sqrt{\frac{3}{2\pi}} \cdot e^{-i\varphi} \cdot \sin \theta = \frac{1}{2} \sqrt{\frac{3}{2\pi}} \cdot \frac{(x - iy)}{r}$$

$$Y_1^0(\theta, \varphi) = \frac{1}{2} \sqrt{\frac{3}{\pi}} \cdot \cos \theta = \frac{1}{2} \sqrt{\frac{3}{\pi}} \cdot \frac{z}{r}$$

$$Y_1^1(\theta, \varphi) = -\frac{1}{2} \sqrt{\frac{3}{2\pi}} \cdot e^{i\varphi} \cdot \sin \theta = -\frac{1}{2} \sqrt{\frac{3}{2\pi}} \cdot \frac{(x + iy)}{r}$$



$l=0 \quad l=1 \quad l=2 \quad l=3$

$m=3$

$m=2$

$m=1$

$m=0$

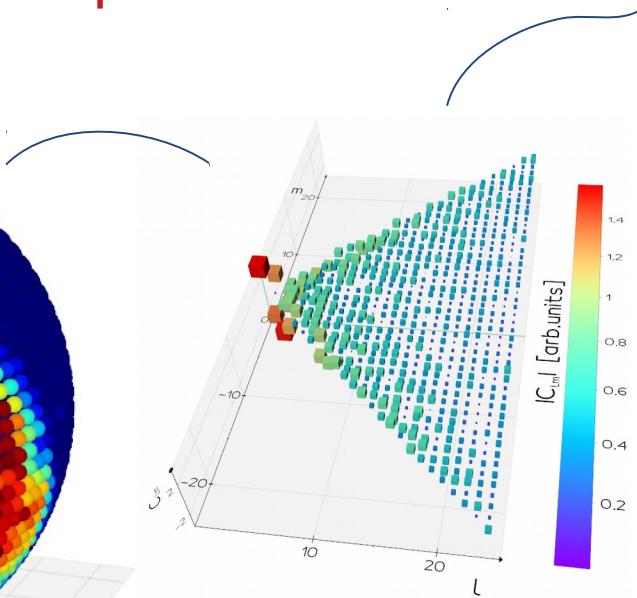
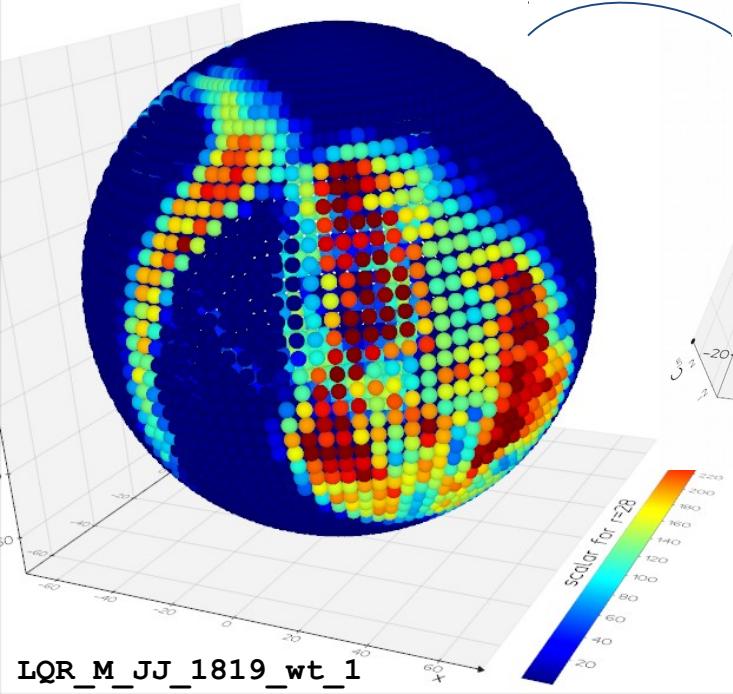
$m=-1$

$m=-2$

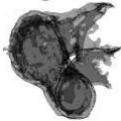
$m=-3$

Used in different fields of science!

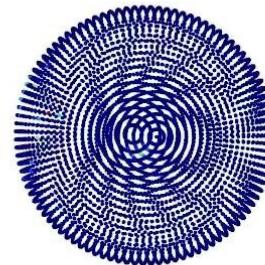
SPH Expansion at specific radius



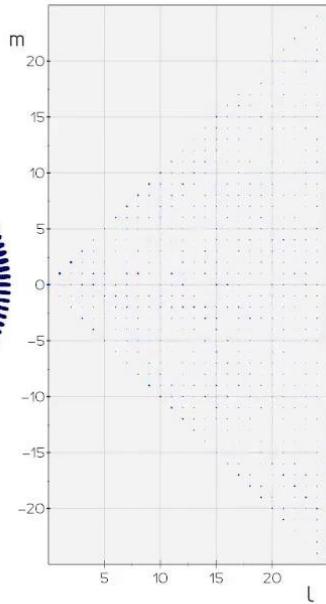
Stage: 2122



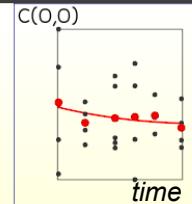
LQR_M_JJ_2122_wt_1



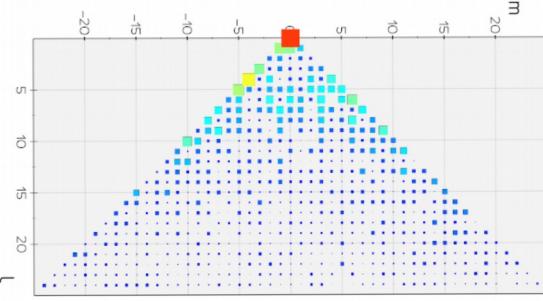
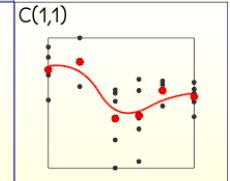
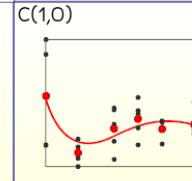
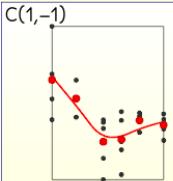
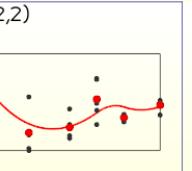
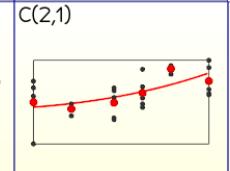
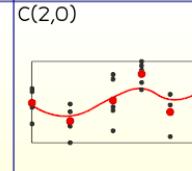
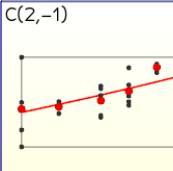
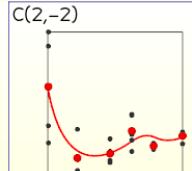
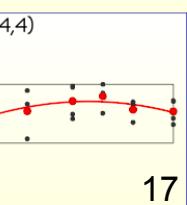
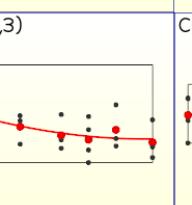
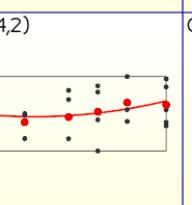
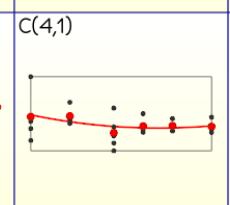
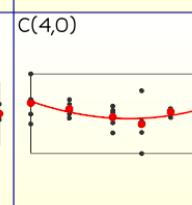
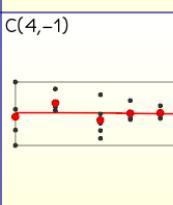
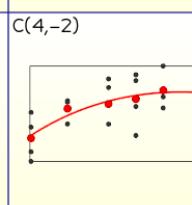
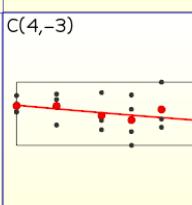
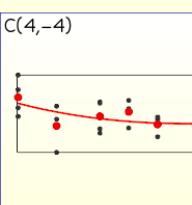
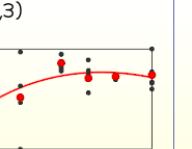
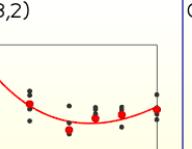
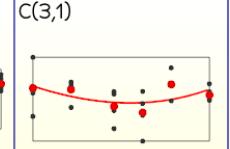
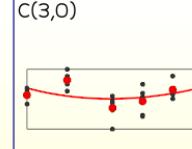
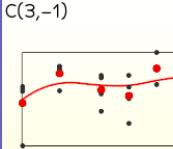
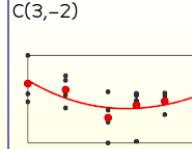
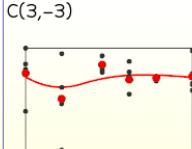
radius = 45

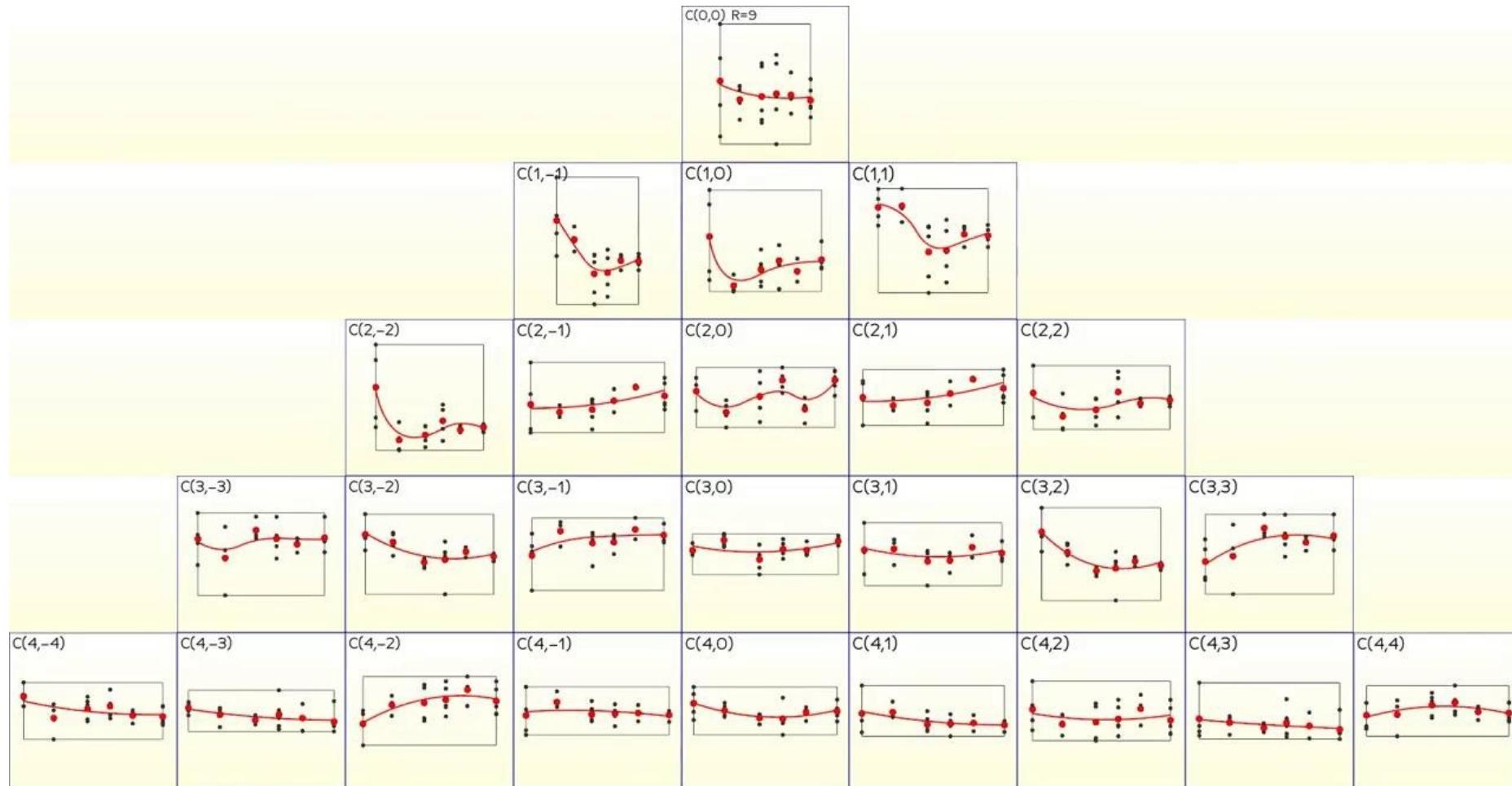


Spherical Harmonics coefficients for shell nr. 10

 $|l|=0$ 

heart $C(l,m)$
ave. $C(l,m)$

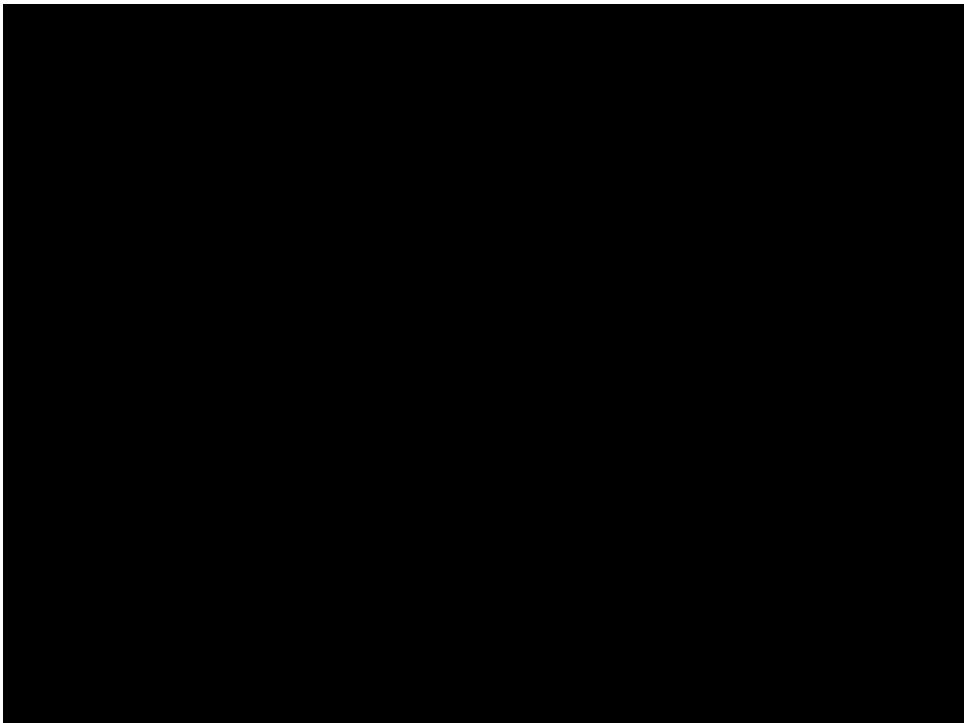
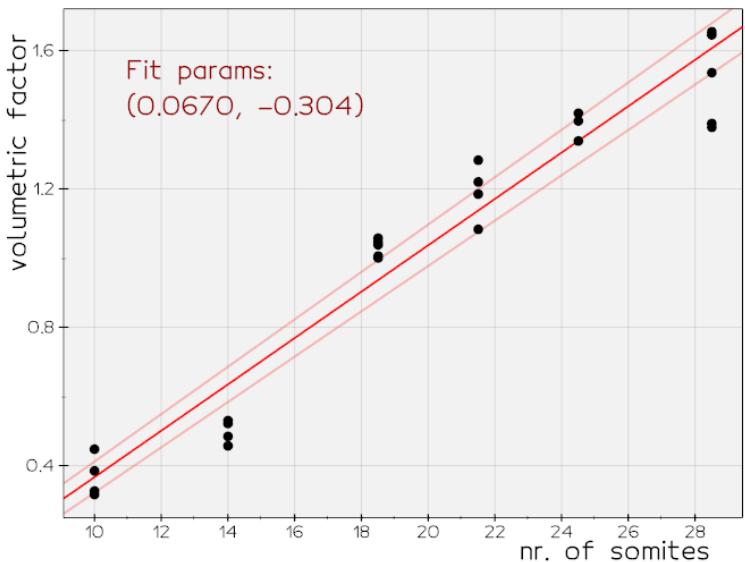
 $|l|=1$  $|l|=2$  $|l|=3$ 



Time Course Results

Wild Type

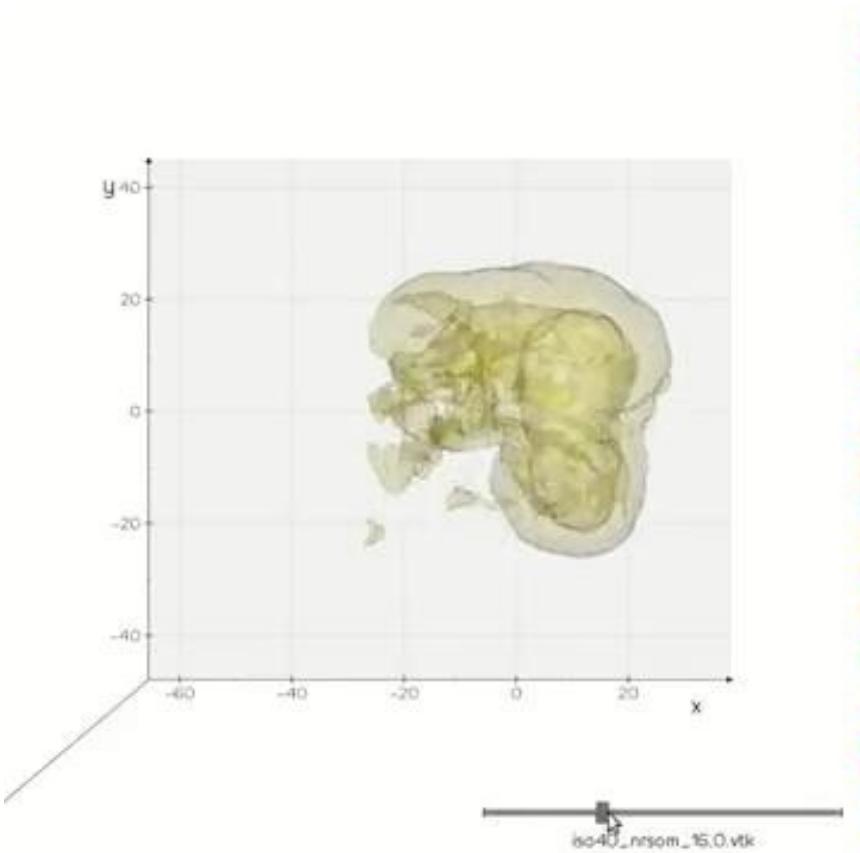
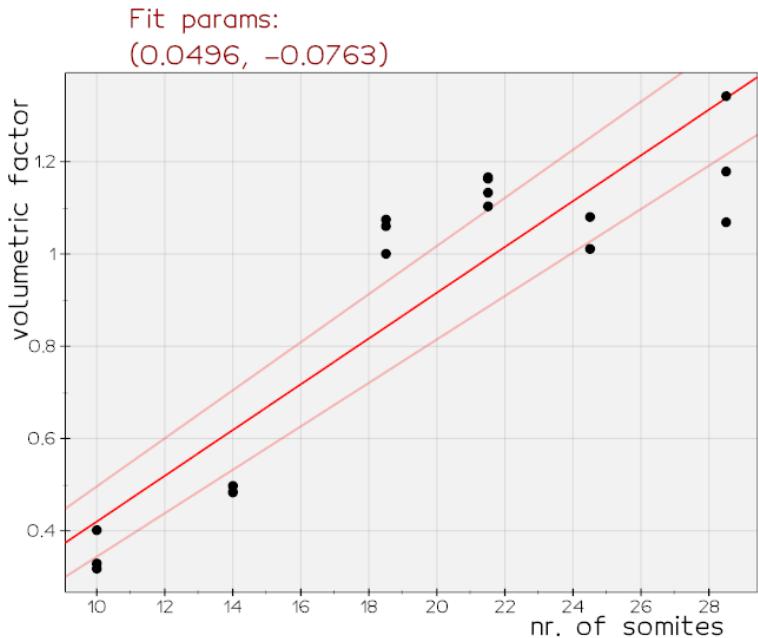
- Recover absolute scale(t)



Time Course Results

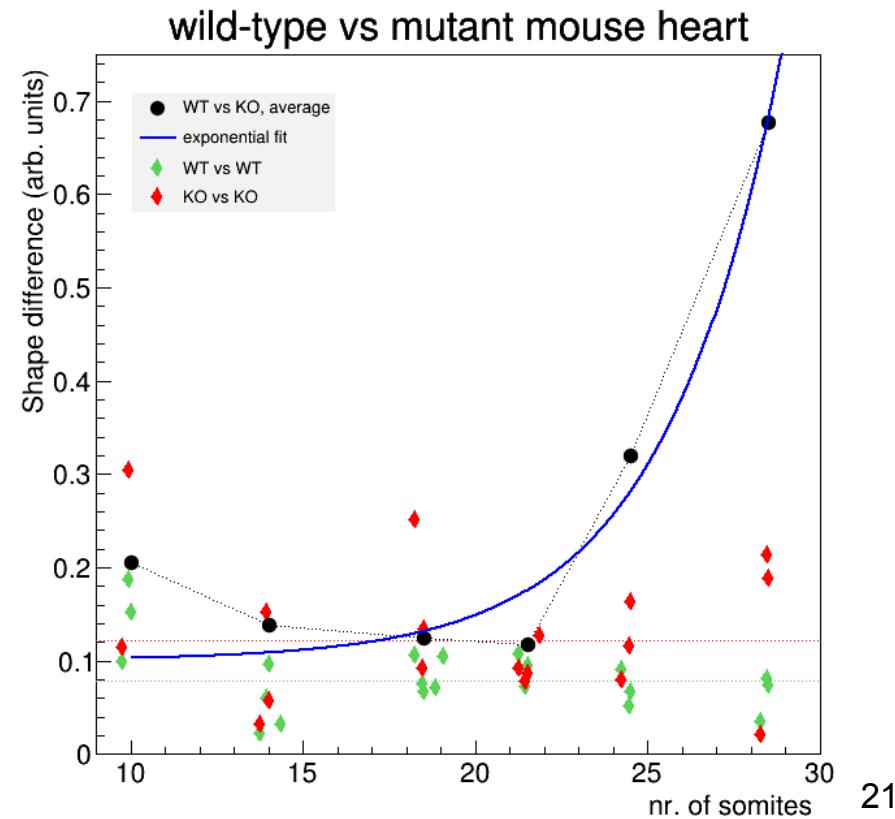
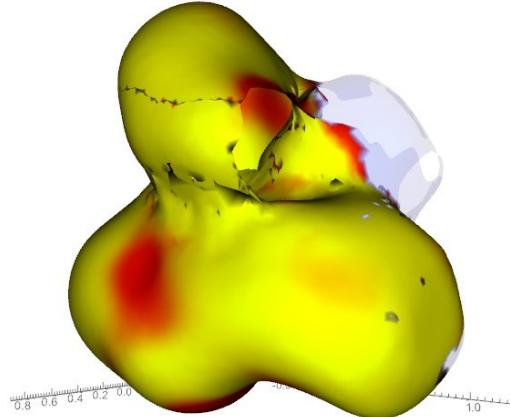
Arid3b - KO

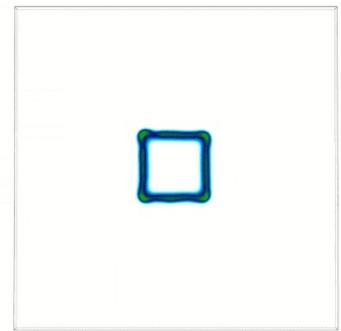
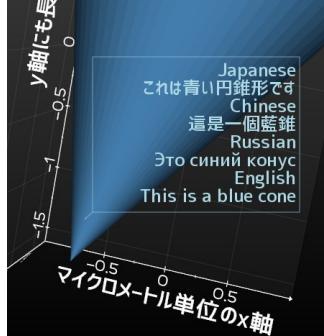
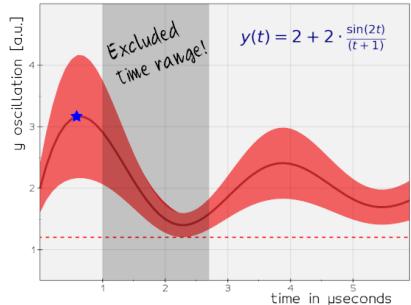
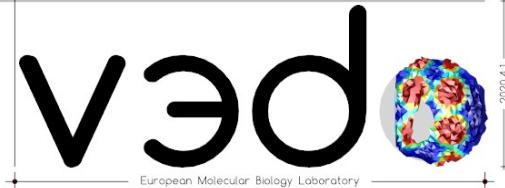
- Recover absolute scale(t)



Global comparison (to be updated)

- Average shapes for each stage by smoothing in 3D point clouds (with Moving Least Squares)
- Compare WT vs KO globally and locally





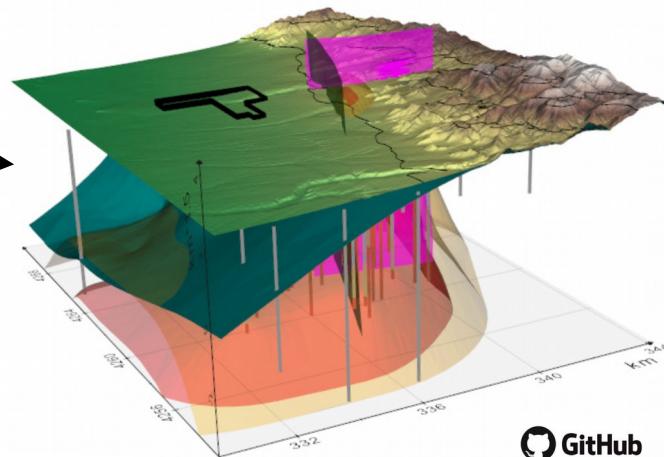
- Name change from “*vtkplotter*”
- Added more features, axes styles, fonts, latex etc
- Export, save and load 3D scenes from file or web link:

```
> vedo https://vedo.embl.es/examples/geo_scene.npy
```



- Not limited to 3D, advanced 2D plotting supported
- Work with meshes, volumes, tet-meshes
- Run 300+ *built-in* examples from command line:

```
> vedo -r grayscott
```



“It's great to see how vedo is becoming even more powerful and mature”, M. Albert - EMBL

“I really enjoy using vedo for making fairly complex models”, A. Pollack – SCRF, Stanford

“..as always vedo makes it so nice to implement new stuff”, F. Claudi – Branco Lab. UCL, UK

“..after playing with it a bit, I was shocked at how easy it is to make very high quality [renderings]”, D. Krsikapa - Queens Univ.



Conclusion

- A preliminary time course of the WT and arid3b-KO hearts is obtained
- Mutants show higher variability in shape and smaller absolute size (~20%)

Next steps:

- Perform some bootstrapping iteration
- Possibly add some morphing with already existing tools
- Update comparison of WT vs KO

Current issues:

- Source volumes are “incomplete”, with parts genuinely missing in data (worth trying some deep learning tech?)
- Some volumes are noisy, with fluorescent parts not in the VOI