

# The Computerized Analysis of Mitochondrial Cristae

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## Introduction

Mitochondria are cellular structures where respiration happens. The necessary chemical reactions take place on the cristae, which are folds in the mitochondrial inner membranes. They provide a large surface area and contain all the protein complexes needed for the reactions. [1]

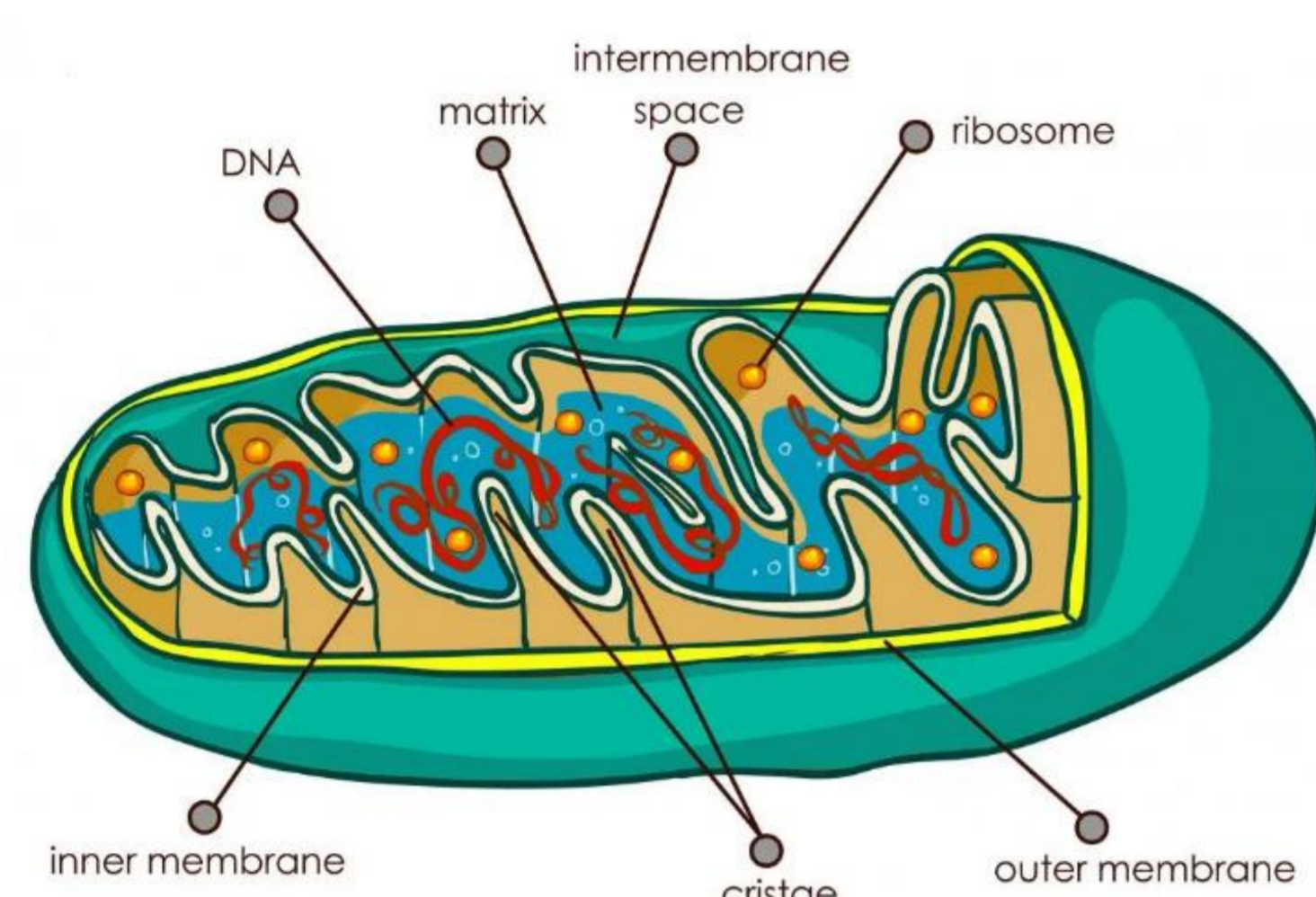


Fig 1: graphical representation of mitochondrial structure [1]

Past studies [2, 3] have shown that mitochondria go through a series of fission & fusion events to allow the transfer/sharing of organelle components. The cristae shape is thus also dynamic and gets remodeled to better adapt.

## Problem

The scientific goal of this study is to investigate the correlation between the cristae's shape features and different cohort groups under various conditions (disease, malnutrition, energy production, etc.)

From a computer science perspective, we would like to eventually develop methods that can better handle anisotropic volumes, such as those obtained from Serial Block-face Scanning Electron Microscopy (SBEM), which is used in biological imaging.

## Materials

The data used for this project are 3D electron microscopy images of mouse brains, curated from a combination of publicly available datasets and private datasets acquired specifically for our purposes.

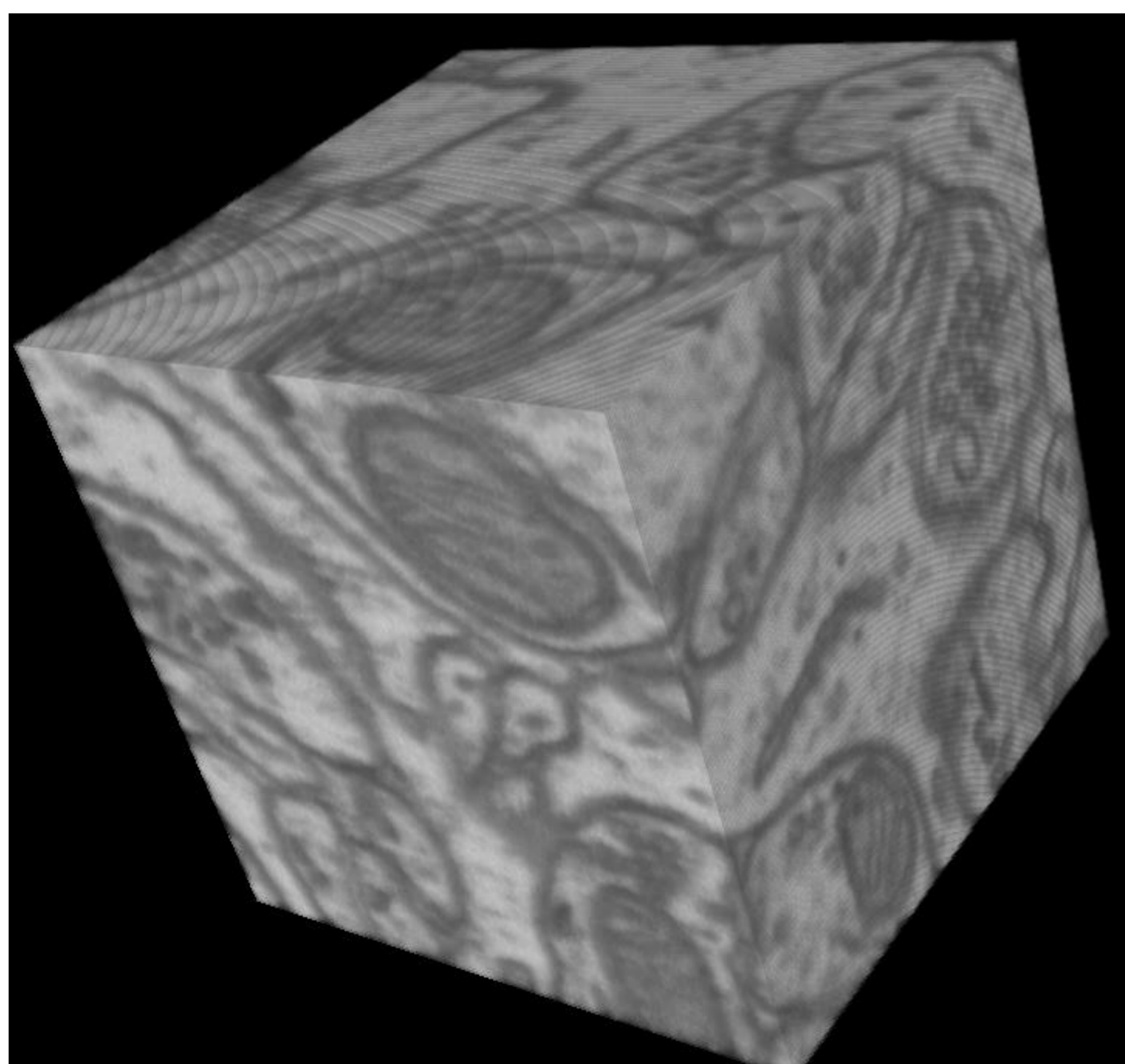


Fig 2: an example of the image volumes used for analysis.

For the first stage of the analysis, we will focus exclusively on images obtained from Focused Ion Beam Scanning Electron Microscopy (FIBSEM), where the image resolution is the same in all 3 axes, to avoid needing to deal with sparse sampling and anisotropy.

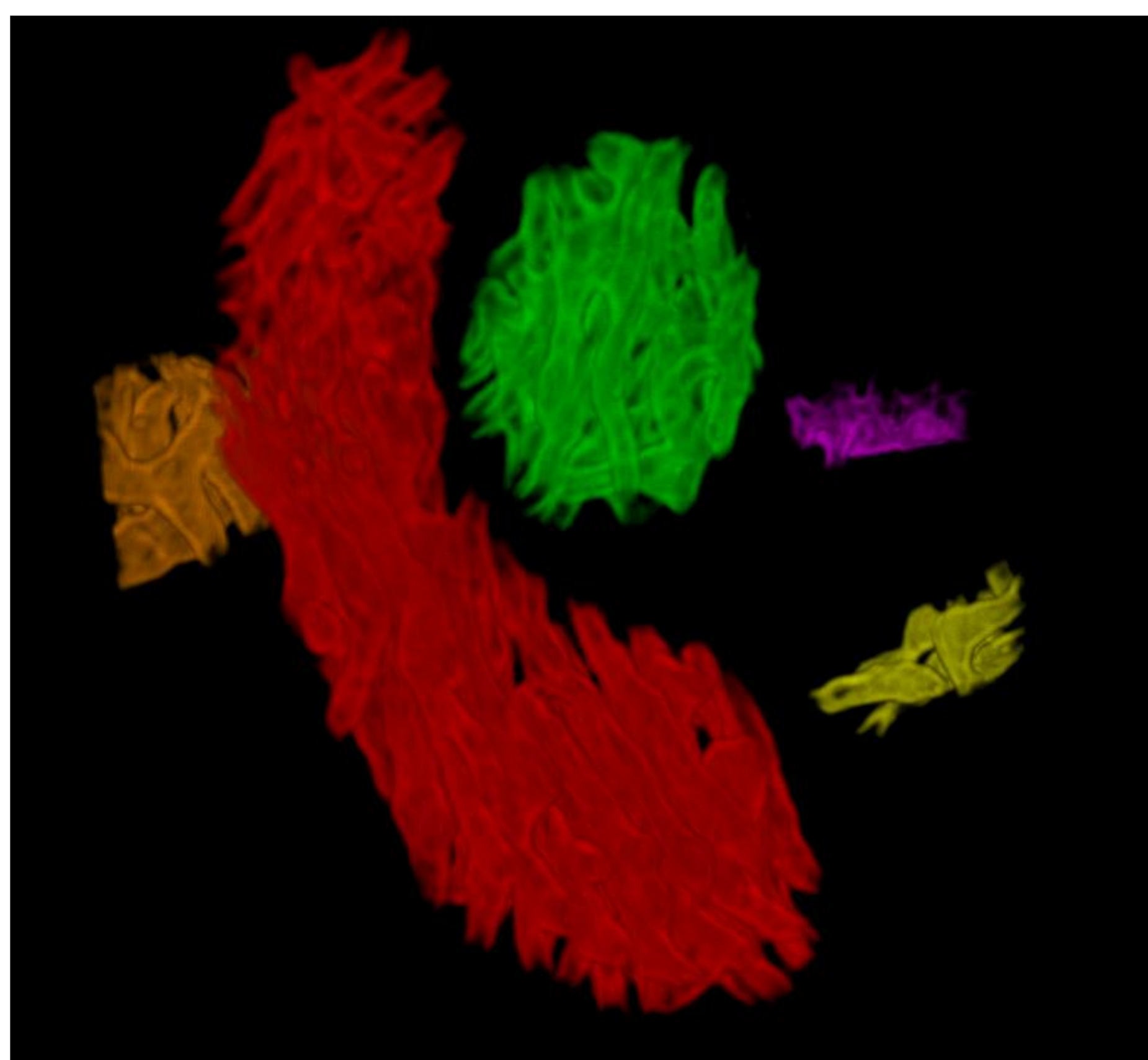


Fig 3: 3D segmentation of the mitochondrial inner membrane.

- 8) Mitochondrial inner membrane lumen volume
- 9) Intermembrane Volume
- 10) Intracristal volume (work in progress)
- 11) Peripheral volume (work in progress)
- 12) Cristal complexity (work in progress)

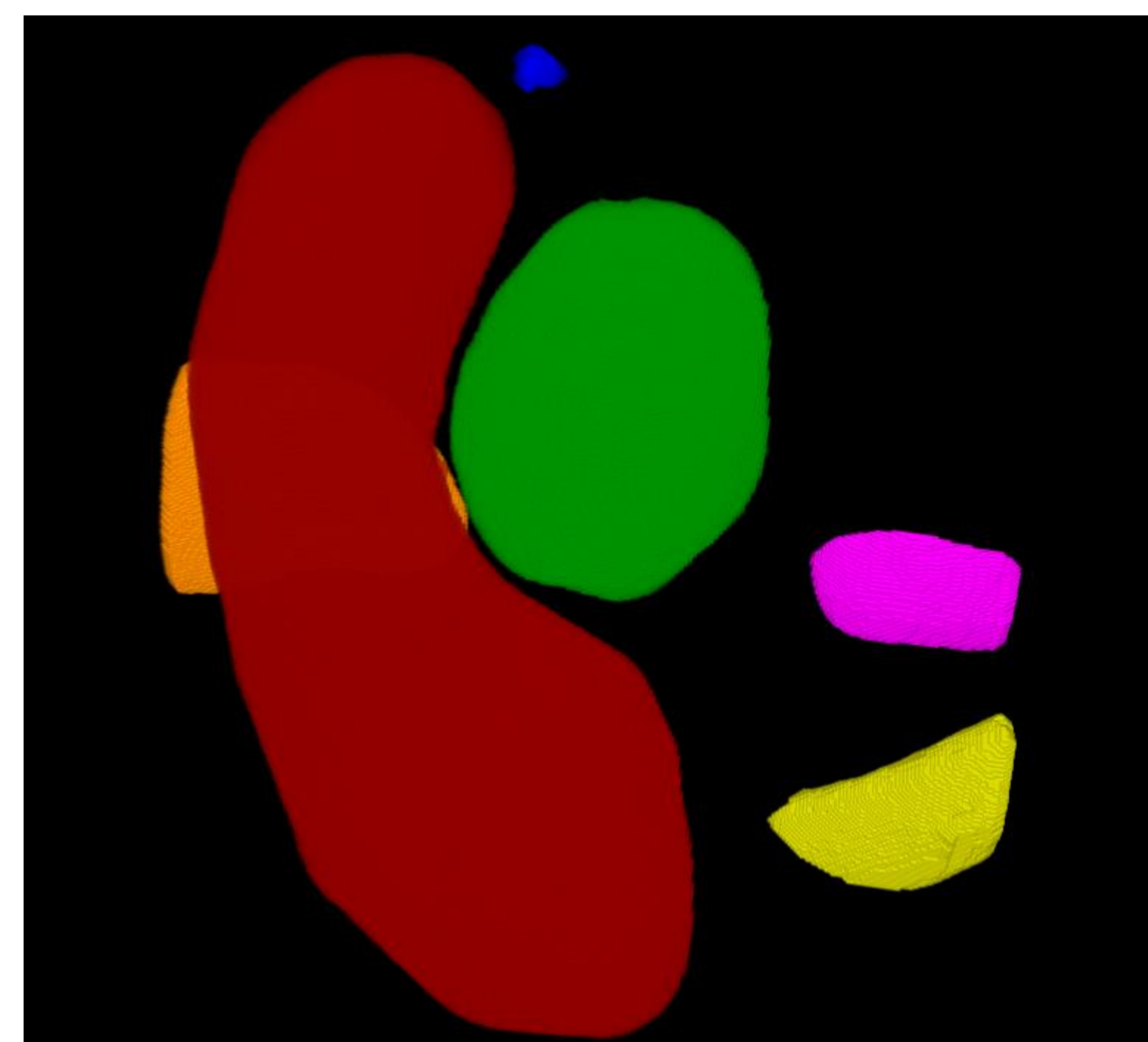


Fig 4: 3D segmentation of the mitochondria.

## Methods

### Segmentation

The first step to the analysis is segmentation. As far as we are aware, there are no publicly available annotations of the mitochondrial inner membrane, so an initial training set needs to be built from scratch. This is done by iteratively annotating the images, predicting with a 2D multiplanar Unet, and then correcting the results.

Once the initial dataset is large and accurate enough, the above is repeated using 3D UNet and continued until the segmentation masks are good enough for analysis.

### Computing the parameters

The segmentation masks of the mitochondrial inner membrane are first multiplied by the 3D connected components of the mitochondria to allow for proper grouping.

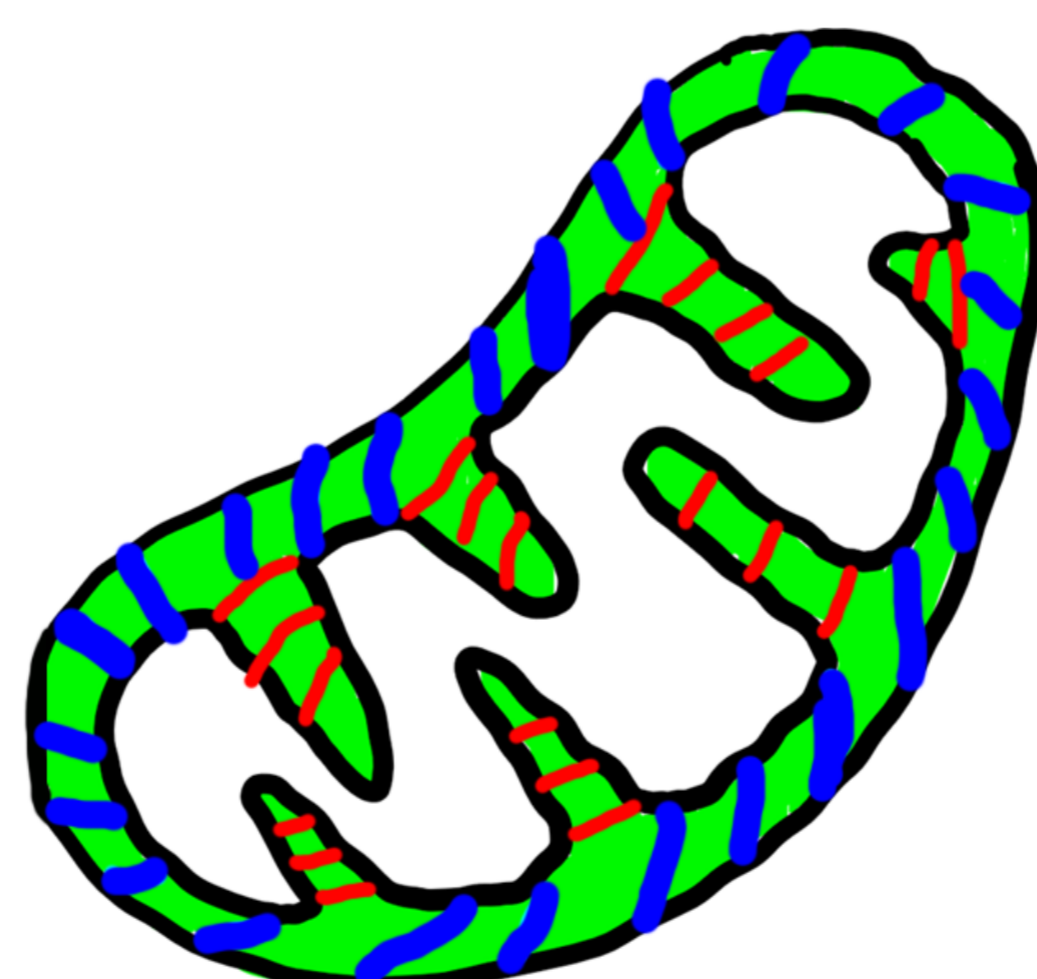


Fig 5: visual explanation of the parameters

The following parameters are then computed:

- 1) Mitochondrion volume
- 2) Mitochondrion surface area
- 3) Mitochondrial inner membrane – total surface area
- 4) Mitochondrial inner membrane – outer surface area
- 5) Mitochondrial inner membrane – inner surface area
- 6) Mitochondrial inner membrane total volume
- 7) Mitochondrial inner membrane volume

Param ID	Blue	Red	Green	Orange	Pink	Yellow
1)	688	1096734	388428	187387	38452	66289
2)	391	71344	28831	14225	4879	7361
3)	0	257868	76494	38000	6301	11038
4)	0	137890	50346	21543	4689	7647
5)	0	119978	26149	16457	1612	3391
6)	0	466589	124379	70359	9432	18427
7)	0	335077	97565	50043	6528	13894
8)	0	131512	26814	20316	2904	4533
9)	0	630145	264049	117028	29020	47862

Table 1: parameter values in voxels, parameter ID corresponds to the numbered list in the previous section.

## Next Steps

- Compare the parametric distributions against the different conditions to check for statistical correlation.
- Start dropping voxels to simulate anisotropy and varying sampling distance, and test how well the existing parameters work. Adapt or develop new feature descriptors that are more robust if necessary.
- Move on to the analysis of 3D images obtained from SBEM, which scans a much larger region at the cost of being anisotropic, where interslice resolution in the z-axis is much lower.

## References

- [1] Newman, T. (2018). What are mitochondria? Medical News Today. Retrieved from: <https://www.medicalnewstoday.com/articles/320875>
- [2] van der Blik AM, Shen Q, Kawajiri S. Mechanisms of mitochondrial fission and fusion. *Cold Spring Harb Perspect Biol.* 2013;5(6):a011072. Published 2013 Jun 1. doi:10.1101/cshperspect.a011072
- [3] Kondadi, A. K., Anand, R., Hänsch, S., Urbach, J., Zobel, T., Wolf, D. M., Segawa, M., Liesa, M., Shirihai, O. S., Weidtkamp-Peters, S., & Reichert, A. S. (2020). Cristae undergo continuous cycles of membrane remodelling in a MICOS-dependent manner. *EMBO Reports*, 21(3). <https://doi.org/10.15252/embr.201949776>