

# Advances in segmented helical reconstruction and insights from oligomeric and polymeric autophagy receptor complexes

C. Sachse

European Molecular Biology Laboratory, Structural and Computational Biology Unit, Meyerhofstr.1, 69117 Heidelberg, Germany, [carsten.sachse@embl.de](mailto:carsten.sachse@embl.de)

Helical protein assemblies present a fundamental architecture of structures involved in diverse cellular processes such as cytoskeleton assembly, endocytosis, signalling and autophagy. I will illustrate based on previous and more recent examples of how direct electron detector technology and image processing have been essential in this method development [1], [2]. Our recent efforts in combining traditional Fourier-Bessel procedures with single-particle algorithms provide a comprehensive approach to structure determination of helical specimens [3]. In my talk, I will present a series of medium to high resolution cryo-EM structures that have advanced our understanding of the molecular mechanism of how cargo is recognized by the selective autophagy machinery. We showed that autophagy receptor p62/SQSTM-1 assembles into flexible helical filaments and provide insights into the molecular basis of polymer formation [4]. EM based structure elucidation in vitro and in situ reveals large oligomeric and polymeric cargo receptor complexes giving rise to higher-order structures that constitute the scaffold for autophagosome formation [5]. The organization of small receptor proteins into helical assemblies provides a cellular mechanism for high selectivity in cargo recognition and a fundamental architecture that enables cargo encapsulation of various sizes from molecular to cellular scale.

## References

{papers2\_bibliography}

- [1] - S.A. Fromm and C. Sachse, "Cryo-EM Structure Determination Using Segmented Helical Image Reconstruction.," *Meth Enzymol*, vol. 579, pp. 307-328, 2016.
- [2] - S.A. Fromm, T.A.M. Bharat, A.J. Jakobi, W.J.H. Hagen, and C. Sachse, "Seeing tobacco mosaic virus through direct electron detectors.," *J Struct Biol*, vol. 189, no. 2, pp. 87-97, Feb. 2015.
- [3] - A. Desfosses, R. Ciuffa, I. Gutsche, and C. Sachse, "SPRING - an image processing package for single-particle based helical reconstruction from electron cryomicrographs.," *J Struct Biol*, vol. 185, no. 1, pp. 15-26, Jan. 2014.
- [4] - R. Ciuffa, T. Lamark, A. K. Tarafder, A. Guesdon, S. Rybina, W. J. H. Hagen, T. Johansen, and C. Sachse, "The selective autophagy receptor p62 forms a flexible filamentous helical scaffold.," *Cell Rep*, vol. 11, no. 5, pp. 748-758, May 2015.
- [5] - C. Bertipaglia, S. Schneider, A. J. Jakobi, A. K. Tarafder, Y. S. Bykov, A. Picco, W. Kukulski, J. Kosinski, W. J. Hagen, A. C. Ravichandran, M. Wilmanns, M. Kaksonen, J. A. Briggs, and C. Sachse, "Higher-order assemblies of oligomeric cargo receptor complexes form the membrane scaffold of the Cvt vesicle.," *EMBO Rep*, vol. 17, no. 7, pp. 1044-1060, Jul. 2016.