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Abstract

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Automatic detection of amyloid fibril crossovers in cryo-EM image data, using a combination of conventional image processing and machine learning

Joint work with A. Bäuerle, M. Schmidt, M. Neumann, M. Fändrich, T. Ropinski and V. Schmidt

Soluble proteins can form insoluble fibers which assemble into so-called amyloid fibrils. Amyloid fibrils are periodically shaped helical structures which cause a group of diseases called amyloidosis when accumulating in organs. Depending on the affected organ, various diseases and symptoms can arise, e.g., heart arrhythmia, kidney disease or Alzheimer's.

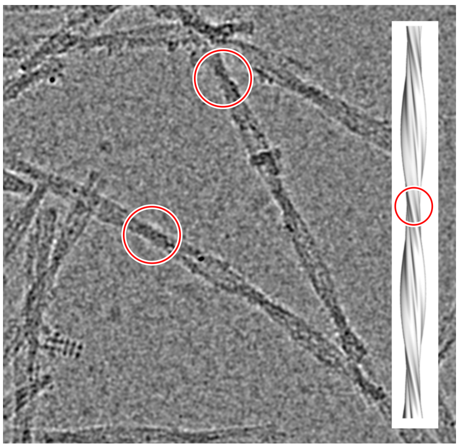

Figure 1: Sample image data of amyloid fibrils obtained by cryo-EM. Segments where the fibril is oriented orthogonal to the image plane, so-called crossovers, are highlighted. Additionally, we show the 3D helical structure of fibrils, leading to the observation of a periodically varying width in 2D.

When observing fibrils using microscopy techniques like cryogenic electron microscopy (cryo-EM), the helical structure results in a seemingly irregular fiber with a periodically varying width. Detecting sections of minimal width (crossovers, see Figure 1) enables us to obtain the pitch of the helix, i.e., the length of a complete turn, by computing the distance between two consecutive crossovers. This is an important characteristic for the analysis of amyloid fibrils.

However, the labeling of crossovers by hand is a time-consuming and error-prone task. We present a method for the automatic extraction of crossovers from 2D image data obtained by cryo-EM. Direct application of convolutional neural networks (CNNs) similar to the U-Net leads to good results when sufficiently good training data is available. In our case, however, many labels are missing in the training data. This leads to various problems which make a direct training and application of a CNN infeasible.

Classical tools of image analysis and pattern recognition like Hough transform and clustering algorithms based on geometric graphs help to mitigate these problems. Thus, we combine classical tools of image analysis and pattern recognition for pre- and postprocessing with machine learning techniques to achieve good results.