In human more than 30 different proteins can misfold and form amyloid. Alzheimer’s disease (AD) and type 2 diabetes (T2D) are common disease where amyloid deposits play an important role in the pathogenesis. In AD, amyloid beta precursor protein (AβPP) deposits in brain and in T2D form islet amyloid polypeptide (IAPP) amyloid in islets of langerhans that leads to destruction of the insulin producing beta cells. [1]

There are mouse and rat models that facilitate studies on AβPP and IAPP aggregation and subsequent development of respective disease, however, it is a long process that extend over many months. Therefore, we and others have established Drosophila melanogaster models that enable studies of amyloid protein misfolding and cellular effects [2].

Structural analysis on the misfolded protein aggregates provide data important for understanding the driving force of protein aggregation and how one protein can adopt different structures dependent on the biological environment. We have applied transmission electron microscopy (TEM) to study the structure of IAPP aggregates formed in Drosophila melanogaster. As shown in figure 1, we detected highly ordered IAPP aggregates in Drosophila melanogaster expressing human IAPP. However, from single 2D TEM image (as shown in figure 1), we are not able to determine the structural information in Z direction. Therefore, we have applied electron tomography technique to study the structural information in Z direction. The tilt series were acquired from 60° to -60°, and double tilt series were carried out in order to minimize the elongation effect in Z direction. [3] The IMOD software was used for image alignment and reconstruction. [4]

In summary, IAPP aggregates detected in the drosophila melanogaster exhibit a spherical shape in the reconstructed tomogram, and spheres are arranged in a body center cubic structure. The individual spheres have a diameter of 17 nm and BCC structure is shown in figure 2 with a distance of 25 nm between.

References
Fig. 1: Figure 1. 2D TEM image of Amyloid peptides aggregates.

Fig. 2: Figure 2. (Left) 2D TEM image of Amyloid peptides aggregates, (Right) Segmented protein aggregates in 3D volume by isosurface method, (Right) showing as BCC structural distribution in 3D. Scale bar is 20 nm.