

LIFE SCIENCE:



Calmodulin is a ubiquitous protein that plays a major role in intracellular signal transduction in most mammalian cells. When the intracellular Ca^{2+} level increase, calmodulin binds Ca^{2+} and then binds to a target protein to modify its function. In the work of Yamada *et al.*, the structural change of calmodulin after Ca binding was studied at a submillisecond time resolution by small-angle X-ray scattering (SAXS) analysis. There were three state-of-the art techniques used in this experiment. One is the high flux beamline BL40XU that provides 10^{15} photons per second. To avoid radiation damage by the intense X-rays, the sample was continuously moved at a speed of 5 cm/s during the X-ray exposure. The second technique was the use of caged Ca that releases Ca^{2+} upon laser irradiation. The third was the X-ray detector that consists of a high-speed (short afterglow) X-ray image intensifier and a fast CMOS camera. By combining these techniques, a continuous time-resolved measurement of calmodulin upon Ca binding was made at a time resolution of 500 μs . As far as I am aware, this is the first time in the world structural change of a protein was continuously followed by SAXS at a time resolution higher than 1 ms. The results showed that calmodulin undergoes a temporary compact conformation within 20 ms after binding Ca, and this conformation is stabilized when calmodulin further binds to a target peptide. This transient state of calmodulin may have significance in cells where the Ca level can fluctuate spuriously.

Tanaka *et al.* from Glico Co. conducted a microbeam diffraction experiment on tooth enamel to investigate the effect of a chemical compound (phosphoryl oligosaccharide, POs-Ca) that is contained in a chewing gum. This compound is hypothesized to bind Ca and maintain a high level of Ca solubilized in the mouth, which facilitates remineralization of caries in the early stage. As expected, in a remineralization experiment on bovine enamel, a solution containing POs-Ca was more effective than just Ca and phosphate. POs-Ca was

MEDICAL BIOLOGY

found to enhance the growth of hydroxyapatite crystallites in enamel. This provides structural evidence of the preventive function for POs-Ca to dental caries.

The phase-contrast CT technique that has been implemented by Hoshino and Uesugi at SPring-8 often produces stunning images of samples. This has already been demonstrated on the eye and brain, but the image of a mouse fetus presented in this volume is also impressive. Developing organs are depicted at high resolution and high contrast. This technique will be useful in detecting defects in transgenic animals. Many genetically modified animals die before birth and it is difficult to determine the cause of death because the fetus is very small and an investigation of the cause requires many pathological sections. By this technique, it is possible to obtain 3D structural information at high resolution, which is useful for finding anomalies during development. This technique has the potential to be used by many researchers in a wide range of fields in biology.

Prof. Matsumoto's group in Osaka University has been working on high-resolution ($3\ \mu\text{m}$) imaging of the structure of bone using monochromatic CT at SPring-8. Its quantitiveness enabled them to estimate the bone mineral density accurately. The results show that vitamin K supplied during the maturation stage may be effective in creating strong bone.

The high flux of SPring-8 helps obtain time-resolved images of a contrast agent flowing through fine blood vessels. The study by Sonobe *et al.* demonstrated, for the first time, that blood vessels in the lung can be visualized in mouse by the angiography technique at SPring-8. The high heart rate (up to 600 beats per min) and small vessel size ($100\ \mu\text{m}$) of mouse require the use of a fast shutter system and a high-resolution imaging detector. Since mouse is often used as a model of cardiovascular diseases, the success of this experiment opens up a new field of circulation physiology.

Naoto Yagi

