Ultra-high Resolution Synchrotron Radiology for Real-time Study

Ever since their discovery by Wilhelm Conrad Rontgen in 1895, medical radiology has been by far the most important application of X-rays. In the overwhelming majority of cases, the contrast in radiological images is based on the different X-ray absorption by different parts of the specimen. Absorption is very limited for X-rays: this is the basis of the striking success of radiology but also of its limitations.

How can we enhance the contrast in radiological images? First of all, we should realize that absorption is not the only type of interaction between X-rays and tissues (or matter in general). Can other interaction mechanisms be used to enhance or replace absorption-based radiology? The answer is positive; the interaction between electromagnetic waves like X-rays and condensed matter is described by the complex refractive index:

$$N(\omega, \mathbf{k}) = n_R(\omega, \mathbf{k}) + i n_I(\omega, \mathbf{k}), \qquad (1)$$

where the imaginary part $n_I(\omega, \mathbf{k})$ corresponds to absorption and $n_R(\omega, \mathbf{k})$ equals the conventional refractive index n in elementary optics. Specifically, n describes phenomena like refraction or diffraction and interference-and in general effects related to phase of the X-ray waves.

In conventional radiology, image contrast is entirely due to the imaginary part $n_I(\omega, \mathbf{k})$, i.e., to absorption. Effects related to $n_R(\omega, \mathbf{k})$, although present in principle, are typically not observable and do not contribute to contrast.

What prevents us from using n-based contrast? The answer is that the corresponding effects are not visible and do not contribute to contrast unless we use coherent X-rays. Refraction-based edge enhancement is essentially due to the fact that different specimen regions with different n-values produce different lateral displacements of a collimated X-ray beam. However, if the entrance and exit specimen surfaces are both flat and perpendicular to the beam, then there is no lateral displacement and no refraction-related edge enhancement.

Consider instead the simple case of Fig. 1 in which an object with a tapered edge is illuminated by a plane-wave X-ray beam (the shading represent the X-ray beam, with the darker areas corresponding to higher intensity). The absorption by the object decreases the beam intensity. Furthermore, the refraction at the edge region deflects the beam by an angle η, whose value depends on the edge slope and on the real part n of the refractive index. The angular deflection η produces a higher-illumination fringe and a darker fringe on the detector.

However, not long ago, coherent X-ray sources were simply not available. The most recent

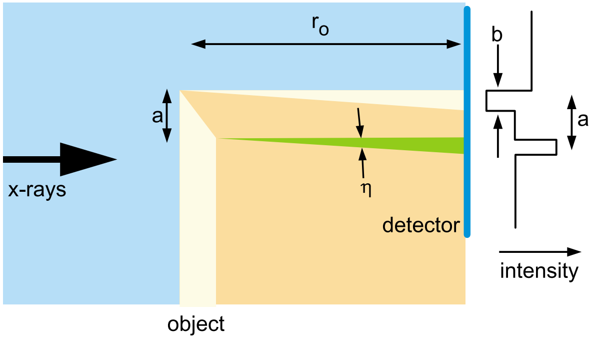

Fig.1: Schematic explanation of the edge enhancement by the "refraction" mechanism.

synchrotron light facilities brought into radiology, for the first time after Rontgen's discovery, highly coherent X-rays. A typical synchrotron light source automatically provides a narrow and collimated beam. This is true for the vertical direction in the case of bending-magnet and wiggler sources and for both directions in the case of undulators. The advanced characteristics of synchrotron X-ray sources make it possible to implement radiology with powerful and innovative approaches.

Biological specimens are prime candidates for phase contrast radiology, in particular because of the possibility to achieve both high lateral and time resolution. Figs. 2 and 3 shows two sets of representative results. The image on the left-hand side of Fig. 2 reveals the microstructure of an ant leg. The top image on the right-hand side is an enlarged portion (bottom left area), demonstrating a lateral resolution of 5-10 μm. This is not the resolution limit of the technique. In fact, the bottom part of the right-hand side of the Fig. 2 shows much better resolution (~2 μm) in the microradiograph of the outer layer of a leaf, taken with similar experimental conditions. The stacking as well as the 2-dimensional arrangement of the cells is clearly visible.

Fig. 3 shows four individual-snapshot radiographs of a live microscopic fish. The exposure time per image was 10 msec. The lateral resolution was 2 μm, similar to the best one of the reference images in Fig. 2. Similarly good images were obtained for a variety of live specimens (under strict and externally monitored experimental conditions as required for this type of tests). The results demonstrate the feasibility of phase-contrast microradiology for animals and human patients.

Medical applications would of course be an intriguing possible development of these techniques. This raises the issue of radiation damage, an issue that deserves further investigation -- although the first tests are quite encouraging. Note, on the other hand, that the contrast mechanism is so effective that the dose can be substantially reduced without seriously jeopardizing the image quality. We did, for example, reduce the radiation dose by partial spectral filtering. Using high quality crystals such as Si as attenuators/filters, we could reduce the total flux density by 2 orders of magnitude and shift the center of the photon energy distribution to 25 keV. This drastically reduced the unnecessary radiation dose.

Radiation damage, in conclusion, does not appear to be a severe problem in view of medical applications. In our opinion, the most serious - but not insurmountable - obstacles for such

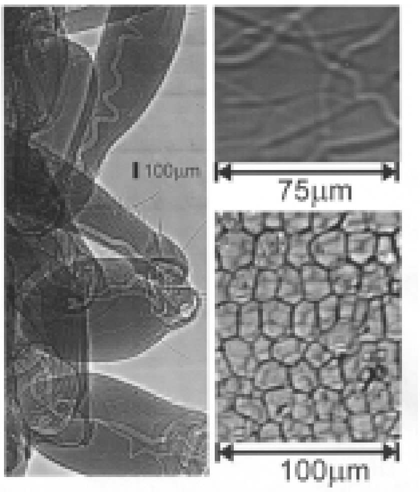

Fig.2: Synchrotron-enhanced microimages of biological specimens. Left: portions of an ant leg. Top right: enlarged part of the same figure. Bottom right: microradiograph of the outer layer of a leaf (taken at SRRC B-20B beamline with lateral resolution of 2 μgm).

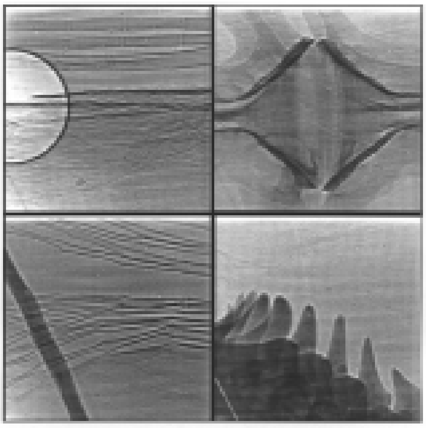

Fig. 3: Microradiographs of a live 15-mm aquarium fish. These are individual pictures (not images extracted from a video tape), with an exposure time per image of 10 msec. The field of view is 300 μgm. The top and bottom-left images refer to the fins on the back and on the tail; the bottom-right image was taken in the branchial region. Note the nearby water bubble in the top-left image.

applications arise from the complexity of the edge-enhanced images. This applies in particular to 3-dimensional tomographic reconstructions. Contrary to conventional radiology, due to phase modulation a phase-contrast radiograph is not simply a projection of the real space structure. Thus, the conventional back-projection tomography algorithm may not reliably yield 3-dimensional reconstructed objects. Substantial efforts are underway to solve this problem, which otherwise could limit the practical biological or medical applications to thin samples.

The applications of phase-contrast imaging in materials research are numerous. For example, electrodeposition is a very widely used industrial technology to grow metals or for metallic coatings, time-resolved experiments are highly desirable to investigate the process dynamics - but also quite difficult and therefore rare. Specific problems are insufficient time resolution to capture the fast evolution, insufficient lateral resolution to reveal the microstructure and insufficient penetration to analyze detailed internal microstructures.

During electrodeposition, the cathode can also generate by water electrolysis hydrogen gas that negatively affects the film quality. Specifically, when too much hydrogen is generated the metal film is usually porous and with poor adhesion. Most researchers attributed this phenomenon to the formation on the electrode of hydrogen bubbles that interfere with the growth. Due to the instability of the bubbles, it is difficult to investigate this mechanism in real time. On the other hand, without sufficient lateral resolution it is difficult to observe the differences in growth morphology and relate them to the bubbles.

As a consequence, previous work on this subject was mostly limited to quantitative measurements of the hydrogen formation and to ex-situ film characterization. A few articles argued on the negative role of hydrogen bubbles, based for example on the observation of bowl and tube shaped voids in the films -- considered as negative bubble fingerprints.

Our experiments, on the other hand, were able to directly link the film growth morphology and the negative effect of hydrogen. Fig. 4 for example, clearly shows the simultaneous formation of metallic zinc dendrites and hydrogen bubbles. Fig. 5 shows further details of the zinc dendrite structure. The most noteworthy point is the direct observation of metal formation on the bubble surfaces. Depending in the experimental conditions, Zn was found on the bubbles as dendrites, films or with other growth forms.

The growth of Zn on hydrogen bubbles leads to the peculiar coating defects that are commonly observed in this and other electrodeposited coatings. Specifically, once the zinc atoms cover the bubble surface, a permanent void of spherical shape is formed that constitutes a coating defect. Our data analysis revealed several important details of the mechanism of Zn growth over the bubbles.

Phase contrast radiology eliminates one of the major handicaps of standard radiology: the use of absorption only to reach contrast. By using contrast based on the (real part of the complex) refractive index, this technique produces images of superior quality with reduced doses and therefore reduced damage. Some of the

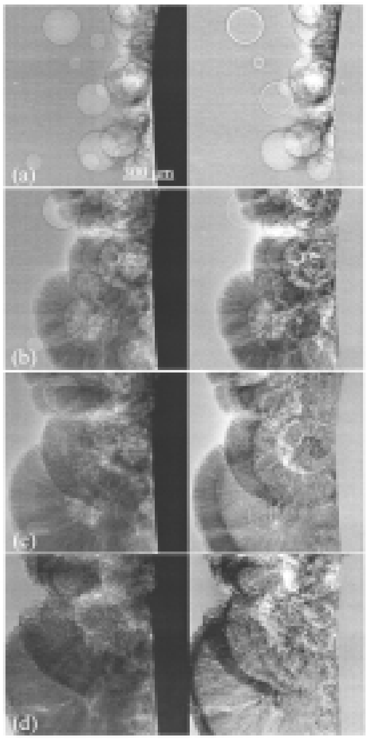

Fig. 4: The sequential images of the zinc dendritic growth from hydrogen bubbles, the time interval between images is 6 seconds.

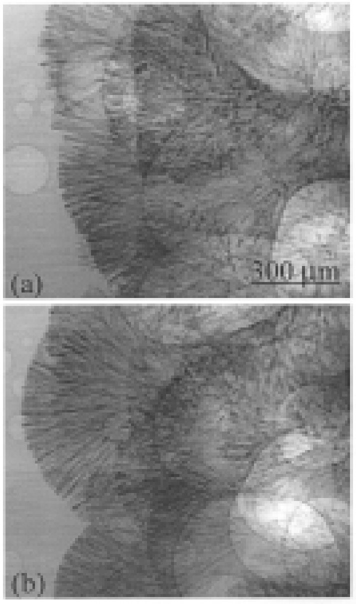

Fig. 5: The details of the zinc dendrites.

improvements in the image quality can be traded against higher lateral and time resolution. The resulting techniques already yielded spectacular results and were used for interesting studies in materials sciences and in the life sciences -- including live specimens. The techniques are particularly important when microscopic and/or dynamic aspects are essential for a specific study.

In the long run, these techniques may find useful applications in medical diagnostics. In that case, they would create a revolution not much different from the initial discovery of X-rays and their almost immediate application to radiology. In essence, phase contrast radiology eliminates a limitation that negatively affected radiology for over a century, making it finally possible to fully unlock its potential capabilities.

Beamline:

20B1 Multi-purpose beamline

Experimental Station:

Phase contrast radiology end station

Author:

Y. Hwu

Institute of Physics, Academia Sinica, Taipei, Taiwan

Publications:

- Y. Hwu, H. H. Hsieh, M. J. Lu, W. L. Tsai, H. M. Lin, W. C. Goh, B. Lai, J. H. Je, C. K. Kim, D. Y. Noh, H. S. Youn, G. Tromba and G. Margaritondo, J. Appl. Phys. **86**, 4613 (1999).
- R. Fitzgerald, Physics Today **53**, 23 (2000).
- Y. Hwu, W. L. Tsai, A. Groso, G. Margaritondo and J. H. Je, J. Phys. D (in press).
- Y. Hwu, W. L. Tsai, B. Lai, J. H. Je, G. H. Fecher, M. Bertolo, G. Margaritondo, Surface Science **480**, 188 (2001).
- W. L. Tsai, P. C. Hsu, Y. Hwu, C. H. Chen, L. W. Chang, H. M. Lin, J. H. Je, A. Groso, G. Margaritondo, Nature **417**, 139 (2002).

Contact e-mail:

phhwu@ccvax.sinica.edu.tw