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Supplementary information

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Phase-contrast calculations

To calculate the signal-to-noise ratio (SNR) due to phase contrast in TEM, consider the average scattering potential for the case of a weak-phase object of thickness *d*. This calculation was originally published[1] in 2003, and the summary included here was recently published[2]. The contrast is calculated at the interface parallel to the beam direction of a nano-object with the surrounding water via the electron scattering factor $f(\theta)$ for scattering angle θ, which is obtained from the scattering cross section[3]:

$$\frac{d\sigma}{d\Omega} = \left| f(\theta) \right|^2 \qquad (1)$$

with scattering cross section σ of one atom and the solid angle Ω. The cross section of elastic scattering based on the Wentzel potential is given by[3]

$$\frac{d\sigma_{el}}{d\Omega} = 4a_H^2 Z^{2/3}(1+E/E_0)^2 \frac{1}{1+(\theta/\theta_0)^2} \qquad (2)$$

where Z is the atomic number, E is the electron energy, a_H *is* the Bohr radius, and the rest energy E_0 is given by

$$E_0 = m_0 c^2 \qquad (3)$$

where m_0 is the rest mass of the electron and c is the speed of light. The characteristic angle is given by[3]

$$\theta_0 = \frac{\lambda Z^{1/3}}{2\pi a_H} \qquad (4)$$

with the relativistic wavelength of the electron defined as

$$\lambda = \frac{hc}{\sqrt{2EE_0 + E^2}} \qquad (5)$$

where h is Planck's constant. The phase contrast amplitude is simply obtained from the zero-angle elastic scattering factor[1] $f(0)$:

$$f_{el}(0) = 2a_H Z^{1/3}\left(1+E/E_0\right) \qquad (6)$$

Scatter-contrast calculations

The basis of calculations of scatter contrast in TEM or STEM use the partial cross section for elastic scattering $\sigma_{el}(\theta)$, which expresses the probability of scattering by an angle θ or larger [2,3]

$$\sigma_{el}(\theta) = (1/\pi)Z^{4/3}\lambda^2(1+E/E_0)^2 \frac{1}{1+(\theta/\theta_0)^2} \qquad (7)$$

1. Rez, P. Comparison of phase contrast transmission electron microscopy with optimized scanning transmission annular dark field imaging for protein imaging. *Ultramicroscopy* **96**, 117-124 (2003).
2. de Jonge, N. Theory of the spatial resolution of (scanning) transmission electron microscopy in liquid water or ice layers. Ultramicroscopy **187**, 113-125 (2018).
3. Reimer, L. & Kohl, H. Transmission electron microscopy: Physics of image formation. (Springer, New York, 2008).