

An efficient thermoelectric material should be a good electronic conductor and a bad thermal conductor. Slack [1] introduced the concept of “electron crystal – phonon glass” to illustrate how such a material could be conceived. Among the classes of materials that fulfill these somewhat contradictory prerequisites and that have been studied extensively are Zintl-phase clathrates, layered main group metal structures and complex antimonides. What these all have in common is a complex crystallography, often caused by a super structure ordering within a simple basic structure. While the average structure forms the basis for the electronic properties of the compounds, and the carrier concentration can be optimized by doping, the super structure order (or disorder) is responsible for lowering the thermal conductivity. The crystallographic challenge lies in elucidating the super structure ordering (commensurate or incommensurate) caused by a relatively small number of scatterers. Since the super structure often adopts a lower symmetry than the basic structure, a frequent further complication is pseudo merohedral twinning, and in more severe cases epitaxial intergrowth between different phases.

[1] Slack, G. A. in *Solid State Physics*, Vol 34, Ehrenreich H., Steitz F., Turnbull D. Eds.: Academic Press, New York, 1979; pp1-71

**Keywords:** thermoelectric; complex structure; intermetallic phases

#### KN-12

**Macromolecular Electron Crystallography.** Jan Pieter Abrahams<sup>a</sup>, Linhua Jiang<sup>a</sup>, Irakli Sikhuralidze<sup>a</sup>, Igor Nederloff<sup>a</sup>, Henny Zandbergen<sup>a</sup>, Dilyana Georgieva<sup>a</sup>. <sup>a</sup>*Leiden Institute of Chemistry, Leiden University, The Netherlands.* <sup>b</sup>*Kavli Institute, Delft University, The Netherlands.*

E-mail: [abrahams@chem.leidenuniv.nl](mailto:abrahams@chem.leidenuniv.nl)

If protein crystals have multiple layers, but are smaller than 1 mm, they are currently beyond the reach of crystallographic structure determination, whether by X-rays or electrons. For structure determination of 3D protein crystals that are smaller than about 0.5  $\mu\text{m}$ , it can be shown that electrons are more suited for structure determination than X-rays, as they are less damaging by several orders of magnitude when normalised to the amount of elastically scattered quanta. Indeed, if only two-dimensional, single-layer crystals of proteins are available, electron diffraction already is the method of choice for structure determination. However, if such crystals have multiple layers, practical problems include the data acquisition, the lack of software to process such data and the absence of successful pilot studies. These drawbacks currently prompt most protein crystallographers into putting their efforts into growing larger crystals that diffract X-rays, and make them abandon projects if such crystals cannot be obtained.

In this seminar, the implications of the fundamental differences between electron refraction and X-ray diffraction of 3D crystals will be discussed and potential solutions to many of the practical problems in electron 3D nanocrystallography will be evaluated. These include

sample preparation and handling routines, data collection strategies, the use of quantum area detectors, data processing software and the potential of novel approaches towards phasing the diffraction data.

**Keywords:** protein crystallography; electron diffraction

#### KN-13

**The Structural Bases of Chromosome Segregation**  
Andrea Musacchio. *Department of Experimental Oncology, European Institute of Oncology, Milan, Italy.*

E-mail: [andrea.musacchio@ifom-ieo-campus.it](mailto:andrea.musacchio@ifom-ieo-campus.it)

Equational division of the genetic material during mitosis is based on the establishment of secure interactions of chromosomes with the mitotic spindle, a microtubule- and motor-based structure [1]. The point of attachment of chromosomes to spindle microtubules is a complex protein scaffold (80-100 proteins) named the kinetochore. Kinetochores can be conceptually dissected into four modules: 1) a DNA-binding module that is built around a specialized nucleosome containing the Histone H3 variant CENP-A; 2) a microtubule-binding module, that is physically tethered to the DNA-binding module, and that is based on a proteinaceous microtubule receptor that goes by the name of the KMN network; 3) an attachment correction module, that removes improper attachments by activating microtubules “saws” such as MCAK and Aurora B; and 4) a safety device known as the spindle assembly checkpoint, that coordinates the chromosome attachment process with a cell cycle oscillator consisting of cyclin-dependent kinases and associated cyclins. Our current challenge is to reduce the functional and structural complexity of kinetochores to a set of basic organizational principles. This requires the construction of an accurate topological map of the kinetochore’s modules, an understanding of their points of contact, and the availability of high-resolution structures of kinetochore components. Our work concentrates on three of the modules (modules 2-4) described above. Specifically, we are applying a combination of structural and functional investigations to unravel the architecture of the microtubule-kinetochore interface (module 2) [2], and its interactions with the error correction mechanism (module 3) [3] and with the spindle assembly checkpoint (module 4) [4]. I will present our main results, and discuss them in the framework of an integrated model of checkpoint function that explains many apparently contradictory aspects of kinetochore biology.

[1] Musacchio A and Salmon ED, *Nat Rev Mol Cell Biol* 2007, 8, 379 [2] Ciferri C, Pasqualato S, Screpanti E, Varetto G, Santaguida S, Dos Reis G, Maiolica A, Polka J, De Luca JG, De Wulf P, Salek M, Rappsilber J, Moores CA, Salmon ED, Musacchio A, *Cell* 2008, 133, 427 [3] Sessa F, Mapelli M, Ciferri C, Tarricone C, Areces L, Schneider T, Stukenberg P, Musacchio A, *Mol Cell* 2005, 18, 379 [4] Mapelli M, Massimiliano L, Santaguida S, Musacchio A, *Cell* 2007, 131, 730

**Keywords:** cell cycle proteins; chromosome dynamics; biological macromolecules