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Acta Cryst. (2011) A67, C147**The structure of conformational junctions in DNA and genomic instability**

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The double helix of DNA, when composed of dinucleotide purine-pyrimidine repeats, can adopt a left-handed helical structure called Z-DNA. For reasons not entirely understood, such dinucleotide repeats in genomic sequences have been associated with genomic instability leading to cancer. Adoption of the left-handed conformation in parts of a long DNA-duplex results in the formation of conformational junctions: A B-to-Z junction is formed at the boundaries of the left-handed helix, whereas a Z-to-Z junction is commonly formed in sequences where the dinucleotide repeat is interrupted by single base insertions or deletions that bring neighboring helices out of phase. B-Z junctions are shown to result in exposed nucleotides vulnerable to chemical or enzymatic modification [1]. We determined and we will describe the three-dimensional crystal structure of a DNA Z-Z junction stabilized by Z α , the Z-DNA binding domain of the RNA editing enzyme ADAR1 [2]. We show that the junction structure consists of a single base pair and leads to partial or full disruption of the helical stacking. The junction region allows intercalating agents to insert themselves into the left-handed helix, which is otherwise resistant to intercalation. However, unlike a B-Z junction, in this structure the bases are not fully extruded, and the stacking between the two left-handed helices is not continuous. The structure captures a dynamic conformational state of the DNA double helix and provides a mechanistic explanation for DNA damage at CpG sites beyond methyl-cytosine modification. Moreover, the structure provides insights on the DNA-binding modes of Z-domains, a family of Z-DNA-binding domains found in interferon response proteins like the DNA sensor DAI and the RNA editing enzyme ADAR1.

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Keywords: DNA structure, conformational junctions, Z-DNA

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Acta Cryst. (2011) A67, C147**Crystal structures of key components in toll-like receptor signaling**

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The Toll-like receptor and IL-1 receptor superfamily (TLR/IL-1R) signals through a number of adaptor proteins and kinases, such as MyD88, IRAK4, IRAK2, TRAF6, and IKK β , to induce nuclear factor κ B (NF- κ B) activation. We here describe the crystal structure of the MyD88: IRAK4: IRAK2 (Myddosome) death domain (DD) complex, which surprisingly reveals a left-handed helical oligomer that consists of 6 MyD88, 4 IRAK4 and 4 IRAK2 DDs [1]. Assembly of this helical signaling tower is hierarchical, in which MyD88 recruits IRAK4 and

the MyD88: IRAK4 complex recruits the IRAK4 substrates IRAK2 or the related IRAK1, consistent with the biology of pathway. Formation of these Myddosome complexes brings the kinase domains of IRAKs into proximity for phosphorylation and activation. Composite binding sites are required for recruitment of the individual DDs in the complex, which are confirmed by mutagenesis and previously identified signaling mutations.

IRAK activation in the TLR/IL-1R pathway leads to subsequent recruitment of the ubiquitin ligase TRAF6 and activation of IKK β . The latter phosphorylates I κ B proteins leading to their degradation and liberation of NF- κ B for gene transcription. We describe the crystal structure of inhibitor-bound IKK β [2]. The structure reveals a tri-modular architecture with the kinase domain (KD), a ubiquitin-like domain (ULD) and an elongated, α -helical scaffold/dimerization domain (SDD). Surprisingly, the predicted leucine zipper and helix-loop-helix motifs do not form these structures but are part of the SDD. We show that a) the ULD is required for catalytic activity; b) the ULD and SDD mediate a critical interaction with I κ B α that restricts substrate specificity, and c) the SDD mediates IKK β dimerization, which is not important for maintaining IKK β activity, and instead required for IKK β activation.

Collectively, these structures highlight the involvement of high order oligomerization in TLR/IL-1R signal transduction.

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Acta Cryst. (2011) A67, C147-C148**Atomic structure, electronic structure and optical response of metal nanoparticles**

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Metal nanoparticles have unique optical properties due to their small size and they are of interest for a variety of applications in devices and materials, including sensing, photovoltaics and optoelectronics. Metal nanoparticles can be fabricated to bridge length scales from small molecular-like structures through to bulk materials in a continuous fashion. Although the optical properties of larger nanoparticles (>2 nm) can be successfully described with classical electrodynamics, for small particles quantum effects become apparent.

This work presents first principles calculations of optimized structures, electronic structure and the optical absorption of gold clusters ranging in size from 10 to over 200 atoms. Ground state properties are calculated using density functional theory (DFT) and the optical response using time-dependent DFT (TDDFT), both within the Octopus code [1]. The largest clusters studied were ~2 nm size and so are in the region where our quantum based calculations should approach the classical results.

The calculations are performed over a discrete grid in real-space and time propagations for TDDFT are performed over discrete steps in real-time. Fully relativistic pseudopotentials were generated under the improved Troullier and Martins method [2] using the Ceperly and Alder local density approximation (LDA) for the exchange-correlation potential [3]. Ground state calculations were made using a Fermi-Dirac type electron smearing to simulate an electronic temperature and to ease convergence of open-shelled systems [4]. Propagations were performed under the LDA and used the approximated enforced time-reversal symmetry (AERTS) method [5]. Approximation of the

exponential of the Hamiltonian was made with the Lanczos method [5].

The optical response of smaller clusters is found to be critically dependent on the atomic structure, even for clusters of the same or very similar size. Very few consistent trends or patterns with size or structure can be identified. The addition of a ligand coating [(PH₃)₁₂Cl₆] to a 55 atom cluster was found to smooth the optical absorption profile, giving better agreement with experimental data. It also reduced the differences between the optical response of structures with a cuboctahedral or icosahedral core.

For the largest structures studied here a convergence in the optical absorption spectra is seen and there is less variation as a consequence of small changes in the atomic arrangements, as we might expect.

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Chemical mapping at atomic-column resolution by STEM-EDX

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Chemical mapping at atomic-column resolution by energy-dispersive X-ray spectroscopy (EDX) in spherical aberration-corrected scanning transmission electron microscope (STEM) was demonstrated in InGaAs, achieving an element-specific resolving power for the dumbbell atomic columns, InGa and As, separated by 1.47 Å. The structural imaging and the chemical information in the two-dimensional map are directly correlated. Comparisons with the other existing mapping technique of STEM in conjunction with electron energy-loss spectroscopy were discussed from aspects of ionization interactions.

Keywords: scanning transmission electron microscopy, energy dispersive X-ray spectroscopy, chemical mapping

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Three-dimensional atomic imaging of crystalline nanoparticles

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Nanomaterials in general and nanoparticles in particular play a key role in modern technology and devices because of their unique physical and chemical properties. These properties are controlled by the exact three-dimensional morphology, structure and composition. Therefore, development of new techniques to determine the structure atom by atom in 3D would allow the properties of the resulting materials to be better understood, increasing the number of applications. The strong interaction of electrons with matter makes electron microscopy

a promising technique to achieve atomic resolution in 3D. Electron tomography enables the recovery of the shape of nanoparticles in 3D from a series of projection images. The resolution that can be obtained in 3D using conventional tomography ranges on the nanometer scale although in 2D atomic resolution has been feasible for nearly four decades. In order to help close the gap between the sub-ångstrom resolution that can be reached in 2D and the coarser resolution in 3D, a new method has been devised combining high-angle annular dark field (HAADF) scanning transmission electron microscopy (STEM), model-based statistical parameter estimation theory and discrete tomography [1].

Discrete tomography [2] has been proposed as a promising technique for atomic resolution tomography in which prior knowledge about the discrete nature of atoms and their lattice structure is exploited. However, an important requirement is that one should be able to determine the number of atoms in each atomic column with great precision from a set of images taken under zone-axis orientations. We therefore employed a quantitative method to analyze HAADF STEM images [3]. It is generally known that such images show Z-contrast allowing one to visually distinguish between chemically different atomic column types. However, if the difference in atomic number of distinct atomic column types is small or if the signal-to-noise ratio is poor, direct interpretation of HAADF STEM images is inadequate. A performance measure which is sensitive to the chemical composition is the total intensity of scattered electrons. These intensities can now be quantified atomic column - by - atomic column using a parametric model describing the contrast of HAADF STEM images. Next, the unknown parameters of the model including the scattered intensities can be estimated by optimizing a criterion of goodness of fit. As such differences in (averaged) atomic number of only 3 can be identified [3]. The high chemical sensitivity is an advantage that could be further exploited to count the number of atoms in a column with an error of only 1 atom. In [1] this method has been proven to work on a metal nanocluster embedded into a stabilizing matrix with the same crystal structure. By counting the number of atoms from two different viewing directions, it has been shown that the three-dimensional structure can be reconstructed at atomic resolution. Recent results show that the method also works for more challenging structures including free-standing nanoclusters.

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Bonding and electronic structure of nanomaterials and interfaces with electron energy loss spectroscopy

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Electron microscopy is an invaluable tool to study the detailed structure of materials. Many of the analytical methods available in the transmission electron microscope, electron energy loss spectroscopy (EELS) in particular, provide detailed compositional and spectroscopic information with unprecedented spatial resolution. In today's modern instruments, energy resolution down to 0.1eV with an electron beams approaching 0.1nm size is possible.

Various examples of applications of electron microscopy will be