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 Zα, 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.

Keywords: DNA structure, conformational junctions, Z-DNA

Crystal structures of key components in toll-like receptor signaling
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The Toll-like receptor and IL-1 receptor superfamilies (TLR/IL-1R) signals through a number of adaptor proteins and kinases, such as MyD88, IRAK4, IRAK2, TRAF6, and IKKβ, to induce nuclear factor κB (NF-κB) 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 IKKβ. The latter phosphorylates IκB proteins leading to their degradation and liberation of NF-κB for gene transcription. We describe the crystal structure of inhibitor-bound IKKβ [2]. The structure reveals a tri-modal 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 IκBα that restricts substrate specificity, and c) the SDD mediates IKKβ dimerization, which is not important for maintaining IKKβ α activity, and instead required for IKKβ β activation.

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

Keywords: biocrystallography, kinase, complex

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-shellled systems [4]. Propagations were performed under the LDA and used the approximated enforced time-reversal symmetry (AERTS) method [5]. Approximation of the
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 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 [IP(3) Cl] to a S5
 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.

 F. Nogueira, A. Castro, M. Marques, in A Primer in Density Functional Theory,
 2004, 121, 3425.

 Keywords: nanocrystal, optical, density functional theory.

 MS.65.2

 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

 MS.65.3

 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-angstrom
 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.

 Dyck, G. Van Tendeloo Ultramicroscopy 2009, 109, 1236-1244.

 Keywords: 3D, electron microscopy, nanocrystal

 MS.65.4

 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