MS10-P7 Comparing electrostatic potentials from experiment, point charges and theory

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A popular analysis for protein structures is the investigation of the electrostatic potential (ESP). It can yield information about possible drug receptor interactions. Therefore, it is also helpful to look at the ESP of a drug molecule. Except for proteins and nucleic acids, charges are not always easily accessible.

This is why we have developed a new, rapid way to a molecular ESP making use of the model compounds in the invariom database [1], for structures of organic molecules. Automatic parameter assignment relies on the local-atomic bonding environment, in this case invariom classification. ESP computation just requires atomic point charges and bond distances to hydrogen atoms from quantum chemistry, and both are provided by the invariom database [1]. These point charges are derived by the RESP [2] procedure for the invariom model compounds and transferred according to invariom name. Hence we call them invariom point charges.

A complementary approach is an ESP from an experimental charge density study, which requires high resolution single crystal X-ray data. Since programs for aspherical scattering factors are complex, we want to asses how well simplified approaches with point charges from different sources can reproduce such an experimental ESP.

A suitable tool for the comparison of ESPs is presented. It is based on MOLISO [3] code and a relative root-mean-square (RRMS) formula known from computational chemistry [4]. Procedures and comparisons will be applied to a series of biologically active organic molecules. ESPs from different methods, including theoretical and experimental charge density, will be compared.

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MS10-P8 BORGES libraries: from phasing to structural bioinformatics

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Despite their differences, *de novo* structure prediction in bioinformatics and *ab initio* phasing methods in crystallography share a common baseline: the use of previous structural knowledge to reveal the tertiary structure of unknown proteins. In phasing, the ubiquitous alpha helices have been widely used as structural building blocks in ARCIMBOLDO_LITE[1]. Nevertheless, some cases require going a step further and moving from secondary to tertiary structure. The emergent strategy, based on fragment libraries as set of initial phases for experimental data, is being the key to success in a number of methods located between Molecular Replacement and pure *ab initio*[2,3,4,5]. Our approach relies on characterization of nonspecific Local Folds[5] as small discontinuous composites of secondary structure elements. Due to their sequence variability, LF can only be evaluated through geometrical descriptors, such as Characteristic Vectors[5], and their spatial constraints. BORGES[5] program implements this idea combining CV geometry, clustering and optimized structural superposition to build user customized LF libraries. The extraction of this kind of libraries requires data mining over more than 100,000 structures deposited in the Protein Data Bank and the design of a specialized database collecting CVs and relations among them. Statistical analysis of LF distribution and pattern recognition studies can only be afforded with the power of a supercomputer, as the one provided by the San Diego Supercomputer Center in California (US)[6], and may reveal interesting features which could augment our structural expertise.

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MS10-P9 Identification and structural modeling of a novel virulence factor from *H.pylori*

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Pathogens produce virulence factors, which help bacteria to invade the host, cause disease and evade host defenses. Recently a class of bacterial proteins which share homology with the Toll/IL-1 receptor (TIR) domain was identified. Those from pathogens; *Brucella* (BtpA and BtpB), uropathogenic *E. coli* (TcpC), *Salmonella* (TlpA) and *Yersinia* (YpTIR) were characterized and their effects on the immune system especially targeting TLR signaling was documented. (*1-5*) BtpA was shown to be directly involved in the virulence of *Brucella* (*5*) and the crystal structure of BtpA confirmed the presence of the TIR domain fold. (*6*). It is yet to be proven if other bacterial proteins with putative TIR domains also function in bacterial pathogenesis. *H. pylori* is a Gram-negative bacteria that colonizes the human stomach and associates with most gastric pathologies, including gastric cancer. *H.pylori* is known for its ability to achieve persistent infection with minimal immune response (7). *H.pylori* might possess a TIR domain containing virulence factor, which can play a role in supressing TLR signaling analogous to BtpA. In order to identify a putative *H.pylori* TIR domain protein, database were searched and HP1437 was found. HP1437, a 239 amino acid protein has a predicted C terminal TIR domain similar to BtpA/TlpA/TcpC and it contains the conserved TIR domain regions. In this study, HP1437 will be characterized using bioinformatic approaches in order to understand its possible role as a bacterial TIR domain protein. The tertiary structure of HP1437 and that of the C terminal TIR domain will be modelled using homology modeling. The structural models with the highest scores will be searched in protein structure database. The structural alignments will reveal the level of similarity of HP1437 to BtpA or other TIR domain protein structures. The results might contribute to our understanding of the reduced immune response to *H.pylori.*

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