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Investigation of different substituents's affects to the crystal and molecular structures in some anesthetic compounds

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In this work, molecular structures of nine local anesthetic compounds have been investigated. These anesthetic compounds are, Bupivacaine, Mepivacaine, Ropivacaine, Lidocaine, Etidocaine, Prilocaine, Procaine, Chloroprocaine, Tetracaine. In the first phase of the research, theoretical and semi-emprical studies have been carried out by using ALCHEMY (MM3-PM3) programs to reach most probable molecular conformations. Some structural knowledge related with Bupivacaine and Mepivacaine have been used as incident information of semi-emprical calculations [1-2]. On the other hand, the effects of different substituents (-CH_3, -OH, -Br, -Cl, etc.) have been investigated in the each of above mentioned compounds. At the end of these studies, chemical diagrams and molecular conformations of new defined anesthetic compounds have been determined. In the second phase, IR, X-ray single and powder diffraction methods were used to see the effect of substituents in the crystal and/or molecular structures. Synthesis of the most probable and new defined compounds have been tried, obtained and common structural information was compared with the help of the first results. The relationship between structure and properties has been tried to explain. Beside these studies, some SAXS models of nano aggregations occurred in the solution of some anesthetic compounds like that of Tetracaine have been constructed and investigated for our next studies on SWAXS applications of local anesthetics [3].

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Accumulation & inversion of the normal matrix using an atomic nearest neighbour sparsity scheme and an analysis of the effect of using such a scheme

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Refinement of meso-molecular structures using the least-squares method produces large matrices which need to be both accumulated and inverted. For the majority of small and meso-molecular structures where m (the number of observations) is much greater than n (the number of parameters), the most demanding part of refinement is accumulation. In these situations, the computations take $O(mn^2)$ to compute, compared with $O(n^3/2)$ for inversion using Cholesky decomposition. We have developed a method of accumulation which uses an atomic nearest neighbour rule to calculate selected important parts of the matrix. This implementation has been very successful, achieving dramatic improvements in the time taken for accumulation (see table).

			$BD^T = A$		
Material	# Params	# Obs	Full	Sparse	A^{-1}
Hen Egg Lysozyme	4620	18994	28:56	1:14	31:50
Hen Egg Lysozyme	3465	18994	16:25	1:01	9:49
Molybdenum Phosphate structure	1766	43783	9:54	0:49	0:55

Table: Timings in minutes of different methods of accumulation

Two aspects of the method will be discussed, the implementation of a fast inversion method which uses the fast accumulation method, and the effect of the sparse accumulation on refinement.
When sparse accumulation is used the inversion soon becomes the most significant part of a refinement cycle. The fast inversion method applies the nearest neighbour rules used in the accumulation to invert the matrix. The implementation of this fast inversion within the program *CRYSTALS*, will be described, along with discussion of the method for re-ordering the sparse matrix to optimise the factorisation, and the effect on the time-cost of the calculation.
The nearest neighbour accumulation method for a structure with a well-conditioned matrix will generally converge towards a minimum. However it has been observed that occasionally once this minimum has been reached, further refinement will cause the structure to diverge catastrophically. An analysis of the differences between a full accumulation and sparse accumulation and a discussion of possible causes and solutions to this problem will be presented.