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Design of highly selective industrial performance chemicals: a molecular modelling approach

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A molecular modelling based approach to design/selection of reagents for industrial applications is presented. The validity and the utility of the proposed approach are illustrated with a case study. The relative strength of interaction of a reagent with inorganic surface is found to correlate well with the experimental trend. The interaction energy thus calculated is utilised as screening tool to identify the most selective reagent for a given surface. Self-assembly of reagents at inorganic–organic interface leads to better selectivity. Wettability of self-assembled monolayers is characterised through contact angle and correlated with experimental results.

Keywords: molecular modelling; performance chemicals; interaction energy; self-assembled monolayers; wettability; contact angle

1. Introduction

Design, development and selection of reagents (surfactants and dispersants) for different industrial applications (mineral processing, ceramics, paints and coatings, cement and nanoparticles) remain an art. Most currently available commercial reagents are selected primarily by trial and error methods based on rules of thumb and past experience. The time and resources required to come up with an acceptable formulation is therefore prohibitively expensive for difficult-to-process systems. Additionally, because of the high cost of empirical search for novel dispersants, the search envelope is severely restricted to a few well-known families of dispersants. A quantitative methodology to screen out/identify the appropriate molecular architectures based on determination of the relative efficacy of various structures derived from theoretical computations, is evidently an economically attractive and elegant methodology as compared to the conventional approach. Selecting the most promising molecules from a wide variety of possibilities based on computer-aided design tools for subsequent synthesis, characterisation, testing and pilot plant/plant trials will certainly save enormous costs in time and efforts to arrive at new formulations.

With recent advances in the understanding of molecular level phenomena governing adsorption of reagents at interfaces, accessibility of application oriented molecular modelling tools and availability of relatively inexpensive computing power, it is possible to design reagents customised for specific applications that are based on theoretical computations. Though there have been isolated attempts in the past to study surfactant–surface interactions using molecular modelling tools [1–11],

a comprehensive methodology to reagent design has been lacking. We have elucidated the building blocks of this novel paradigm through our recent publications on this topic [12–22]. Two key features of the proposed approach are: (i) identification of the molecular recognition mechanisms underlying the adsorption of reagents at the interface and (ii) use of advanced molecular modelling techniques for theoretical computations of the relative magnitude of interaction. The molecular modelling thus provides a quantitative search technique for screening and identifying the most promising molecular architectures from a large set of candidates available for a particular application. As a consequence, considerable saving in time and effort needed for developing new formulations is possible.

In this paper, we present a brief overview of this rational design paradigm through a case study drawn from our work on separation amongst calcium minerals.

2. Methodology

Universal force field (UFF) [23–26] as implemented in Material Studio[®] (MS; [27]) has been used to model the inorganic surface–reagent interactions. We have successfully demonstrated through our earlier work that UFF can be used to model the mineral–reagent systems with reasonable accuracy [16–19]. A detailed methodology of modelling the mineral–reagent interactions has been reported earlier [16]. The geometry of reagent molecules (surfactant/dispersant/flocculant) was optimised using UFF as implemented in forcite module of MS. A surface cell was created from the unit cell of the inorganic crystal

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at its cleavage plane and optimised with the help of surface builder module in MS. The optimised reagent molecule was docked on the mineral surface. The initial geometry of surface–reagent complex was created physically on the screen with the help of molecular graphics tools, taking into consideration the possible interactions of reagent functional groups with surface atoms. The reagent molecule was then allowed to relax completely on the surface using forcite geometry optimisation. Several initial conformations (~ 20) were assessed so as to locate the minimum energy conformation of the inorganic surface–reagent complex. The partial charges on the atoms were calculated using charge equilibration method [28]. The intra-molecular van der Waal interactions were calculated only between atoms which are located at distances greater than fourth nearest neighbours. A modified Ewald summation method [29] was used for calculating the non-bonded coulomb interactions while for van der Waal interactions a direct cut-off at a distance less than $r/2$ (where r is the length of the simulation cell) was employed. Smart minimiser as implemented in forcite module of MS was used for geometry optimisation. The optimisation was considered to be converged when a gradient of 0.0001 kcal/mol is reached. The interaction energy was calculated for the most likely/favourable conformation using the following equation:

$$\text{interaction energy}(\Delta E) = E_{\text{complex}} - [E_{\text{reagent}} + E_{\text{surface}}], \quad (1)$$

where E_{complex} , E_{reagent} and E_{surface} are the total energies of optimised surface–reagent complex, reagent molecule and surface cluster, respectively.

Structure of the complex obtained through static energy minimisation method represents only a local minimum energy structure; it was further optimised to find a global minimum energy structure through molecular dynamics (MD) simulations (both in vacuum and presence of the solvent) using forcite dynamics. MD calculations were run using constant energy microcanonical ensemble method (NVE) at 300 K with time step of 1 fs. Total run length was ~ 300 ps. During the simulations, the temperature was controlled by velocity scaling method. During simulations, atom-based cut-off method was employed for calculating both Van der Waals and electrostatic forces. The interaction energies were computed as:

$$IE_{(\text{in solvent})} = \Delta E_{\text{combined}} - \sum (\Delta E_{\text{solvent-reagent}} + \Delta E_{\text{surface-solvent}}), \quad (2)$$

$$\Delta E_{\text{combined}} = E_{\text{complex, solvent}} - \sum (E_{\text{surface}} + E_{\text{reagent}} + E_{\text{solvent}}), \quad (3)$$

where E_{combined} is the total interaction energy calculated using Equation (3). $E_{\text{complex, solvent}}$ is the total energy of the optimised surface–reagent complex in the presence of solvent, E_{surface} , E_{reagent} and E_{solvent} are the total energies of free surface, reagent and solvent molecules, computed separately. $\Delta E_{\text{solvent-reagent}}$ is the interaction energy computed for the interaction of solvent and reagent molecule and $\Delta E_{\text{surface-solvent}}$ is the contribution due to interaction of solvent molecules with the surface. These energies are subtracted from $\Delta E_{\text{combined}}$ to get the final interaction energy [$IE_{(\text{in solvent})}$] of reagent molecule with the inorganic surface (Equation (2)). It is worth noting that the more negative magnitude of interaction energy indicates more favourable interactions between the reagent and inorganic surface. The magnitude of this quantity is thus an excellent measure of the relative intensity/efficiency of interaction amongst various reagents.

For modelling self-assembled monolayers (SAMs), a monolayer of reagent molecules was placed on the inorganic surface. The reagent molecules were placed as per the most stable conformation obtained through optimised single molecule–surface complex. In order to find the equilibrium structures of the adsorbed monolayers, the clusters thus created were subjected to geometry optimisation followed by MD simulations at 300 K. The surface atoms were kept fixed during the entire simulation run and only adsorbed reagent molecules were allowed to relax.

For simulating wetting behaviour of SAMs, a water droplet was placed at the surface and equilibrated using MD simulations. To create a water droplet of experimental density, first a 3D-periodic box containing 512 water molecules was equilibrated at 300 K using MD simulations. A sphere of 20 Å radius (329 water molecules) was cut out of this 3D-periodic box and placed over the SAMs. The system was equilibrated using MD simulations and during entire MD run inorganic surface atoms were kept fixed. The methodology proposed by Fan and Cagin [30] was utilised to extract the microscopic parameters namely the drop volume (V) and the interfacial area (S) of water droplet which was then put in Equation (6) to calculate contact angles.

The height of the droplet (h) from the terminal methyl layer and the radius of the droplet (R) are calculated as follows:

$$h^3 + 3S h/\pi - 6V/\pi = 0, \quad (4)$$

$$R = h/2 + S/2\pi h. \quad (5)$$

The contact angle (θ) is related to the height and the droplet radius as shown below:

$$\cos \theta = 1 - h/R. \quad (6)$$

3. Results and discussions

3.1 Selective collectors (surfactants) for separation amongst calcium minerals

The separation of sparingly soluble calcium minerals, such as fluorite (CaF_2), calcite (CaCO_3), fluorapatite ($\text{Ca}_{10}(\text{PO}_4)_6\text{F}_2$), dolomite [$(\text{Ca}, \text{Mg})\text{CO}_3$] and scheelite (CaWO_4), from each other remains a challenging problem without a satisfactory solution till date. The difficulty arises out of their similar surface properties and solubility, same chelating cation (Ca) in their structure and similar response to various known families of flotation collectors like fatty acids. Many possible hypotheses have also been suggested in literature to explain this observation [31–35]. We have applied molecular modelling methodology to design more selective collectors for their separation [16,17]. As shown in Figure 1, diphosphonic acid based collectors are found to be more effective than conventional fatty acids [16]. The order of selectivity, as predicted by theoretical computations (interaction energies), compares very well with experimental flotation response of these reagents. We utilised this methodology further to design selective depressants for beneficiation of difficult to process phosphate ores (separation of calcite/dolomite from fluorapatite) (Indian Patent Application No. 132/MUM/2005 & 133/MUM/2005).

3.2 Conformation of adsorbed molecule

Another aspect of these computations was to obtain the most favourable configuration of the adsorbed molecule on a given inorganic surface. The theoretical results were validated with experimental data. For example, as observed in experimental investigations, two most stable fluorite–oleate complexes namely, uni- and bi-dentate, were predicted through molecular modelling calculations as well [36]. As shown in Figure 2, the theoretically simulated conformation (as indicated through adsorption angles [36], matched well with experimental one (obtained through a sophisticated *in situ* infrared external reflection spectroscopy technique [37]).

3.3 Self-assembled monolayers

Interaction energies computed on the basis of single reagent molecule adsorbing on the inorganic surface does provide a very useful quantitative and theoretical measure for assessing the relative affinity of various surface–reagent combinations. Such computations are therefore very useful inputs in the design/screening of different molecular architectures for a given separation system. These computations, however, do not capture the associative interactions amongst the adsorbed molecules. In order to study the structure of the adsorbed monolayers so as to delineate the more subtle template effects

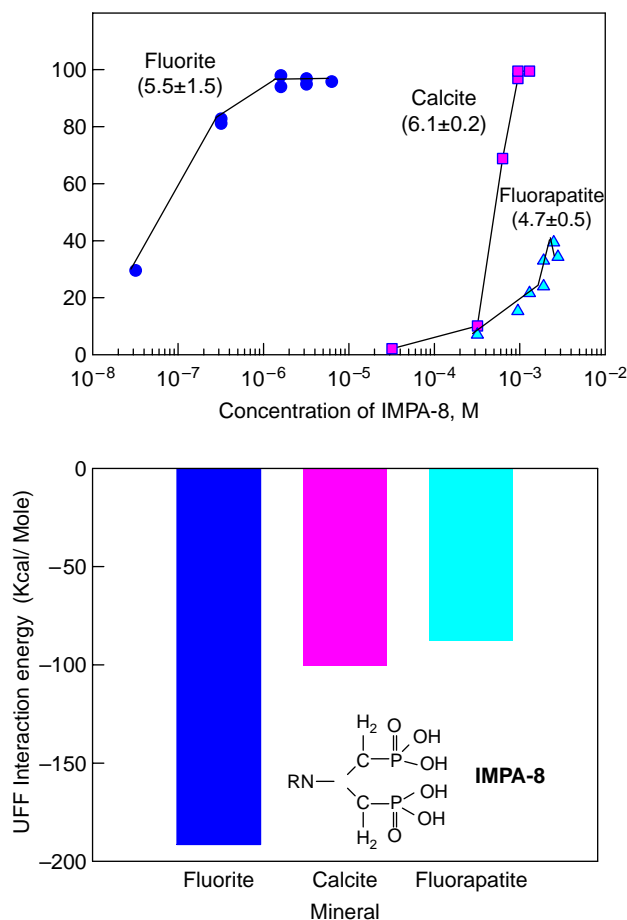


Figure 1. Comparison of experimental flotation results for the most selective phosphonic acid reagent (octyliminobismethylene phosphonic acid IMPA-8) with its computed interaction energies at different mineral surfaces (after [16]).

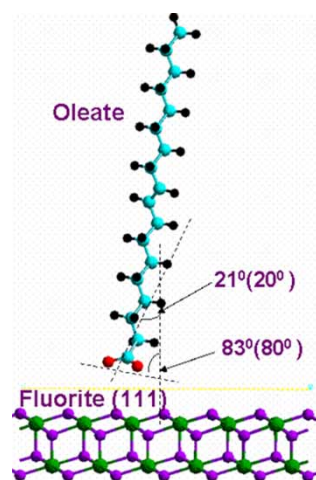


Figure 2. Conformation of adsorbed oleate molecule on fluorite surface. The numbers in bracket denote experimental angles obtained through *in situ* infrared external reflection spectroscopy technique (after [36]).

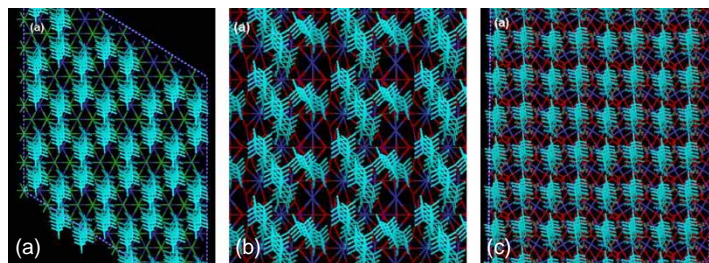


Figure 3. Structure of adsorbed oleate SAMs on (a) fluorite, (b) fluorapatite and (c) calcite surfaces (after [22]). [Graphical displays generated with Materials Studio].

of the substrate in determining the macroscopic behaviour of the reagents in actual application, we have also simulated adsorption of several molecules together on the surface, leading to well-defined monolayers. More detailed information on the most likely structure of the adsorbed monolayers was obtained.

We have modelled SAMs of conventional fatty acid (oleate) molecule on calcium mineral surfaces [22]. Different coverage's, in terms of site occupancy, leading to different structures were modelled (Figure 3). On fluorite surface the most favourable conformation was found to be with oleates adsorbed in a hexagonal lattice (67% coverage). The coverage area per molecule (22.2 \AA^2) for this conformation matched closely to oleate molecular area (20 \AA^2). Whereas on calcite surface 100% coverage was possible with computed area (20.2 \AA^2) matching to that of oleate molecule. On fluorapatite surface best fit was obtained with 75% occupancy leading to matching computed area per molecule (21.5 \AA^2).

3.4 Wettability of SAMs

Based on the results of adsorbed SAMs, calcite was found to be the best template for oleate adsorption however; fluorite is most responsive to experimental flotation with oleate (Figure 5). Since the flotation is directly related to wettability of adsorbed SAMs, which is quantified using contact-angle measurements, we also computed contact angle of water droplet placed on the adsorbed SAMs at different inorganic surfaces. As shown in Figure 4, oleate SAM adsorbed on the fluorite surface seems to be more hydrophobic as compared to those adsorbed on calcite or fluorapatite surfaces. Thus, even though calcite tend to be the best template for adsorption, the wetting characteristics of adsorbed SAMs predict better floatability for fluorite in presence of oleate. Indeed, it is heartening to note that experimental flotation response follow the same order as predicted by wettability (contact angle) simulations (Figure 5).

4. Concluding remarks

The utility of currently available molecular modelling tools in the design and screening of reagents for industrial

applications is demonstrated through this communication. Even though this paper deals with reagents for mineral separation system, the proposed molecular modelling based theoretical approach is very generic in nature and provides a scientifically robust framework for the design/selection of appropriate reagent and/or solvent for a given application. With steady advancements being made in the theory and practice of molecular modelling approach, it is anticipated that even more complex design problems can be solved, in particular with respect to the optimisation of the molecular architecture in order to develop performance chemicals tailor-made for the desired application.

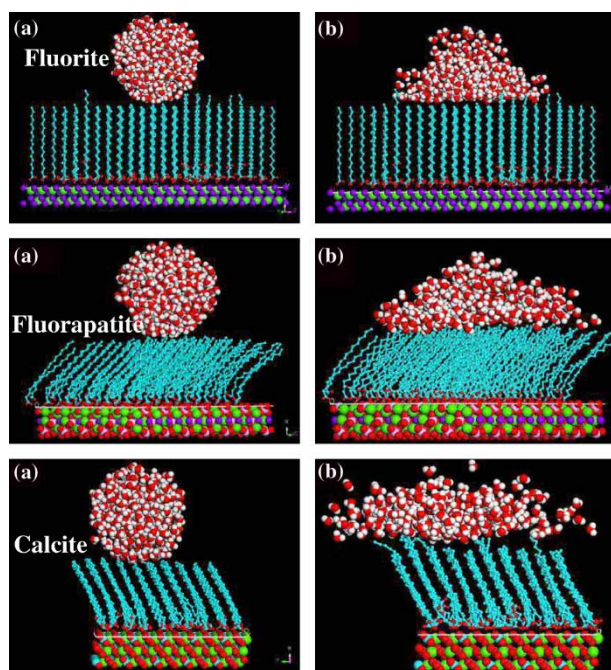


Figure 4. Snapshots of a water droplet on adsorbed SAMs on fluorite, fluorapatite and calcite surfaces (a) before equilibration (b) after 300 ps of MD run. [Graphical displays generated with Materials Studio].

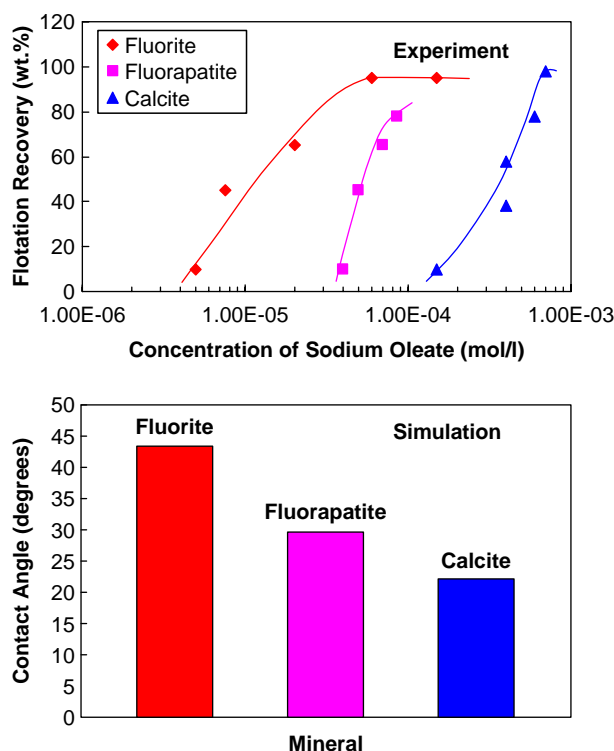


Figure 5. A comparison of computed contact angles with experimental flotation response of oleate with different calcium minerals. (Experimental flotation data taken from [31]).

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