# QUANTITATIVE STRUCTURAL ACTIVITY RELATIONS (QSAR) OF COMPOUNDS

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**Abstract** QSAR techniques are used to explore the relationships of computer technology, mathematical and computational models for analysis, modeling and predicting toxicological effects using chemical structural descriptors and various endpoints. Pattern recognition techniques and other principal component analysis are then used to further explore the mechanisms of toxicity. The present study is limited to modeling of Hemoglobin using Chimera. Other investigations with different classes of pharmaceutical compounds and medical devices are ongoing. It is proposed that similar techniques may be explored to predict better molecules that may be used to obtain low voltages and other energy saving devices.

## INTRODUCTION

Running an experiment in silico, that is, computer simulation, has its advantages and disadvantages. In silico experiments may provide energertics or spectroscopy of a molecule using quantum chemical computational techniques. Such calculations may provide an idea of the motion of electrons in the atoms of the molecules. The Born-Oppenheimer (BO) approximation may be used.

Within the BO approximation the Hamiltonian, or total energy operator, for a molecule with $M$ nuclei and $N$ electrons is

$$\hat{H} = \underbrace{-\sum_{i=1}^{N}\frac{\hbar^2}{2m_e}\nabla_i^2}_{\text{electron kinetic energy}} + \underbrace{\frac{1}{2}\sum_{a=1}^{M}\sum_{b\neq a}\frac{Z_a Z_b e^2}{4\pi\epsilon_0|\vec{R}_a-\vec{R}_b|}}_{\substack{\text{nuclear-nuclear}\\ \text{Coulomb repulsion}}} - \underbrace{\sum_{a=1}^{M}\sum_{i=1}^{N}\frac{Z_a e^2}{4\pi\epsilon_0|\vec{R}_a-\vec{r}_i|}}_{\substack{\text{electron-nuclear}\\ \text{Coulomb attraction}}} + \underbrace{\frac{1}{2}\sum_{i=1}^{N}\sum_{j\neq i}\frac{e^2}{4\pi\epsilon_0|\vec{r}_i-\vec{r}_j|}}_{\substack{\text{electron-electron}\\ \text{Coulomb repulsion}}}, \quad (1)$$

where $Z_a$ is the nuclear charge of nucleus $a$ (*e.g.* $Z_a = 1$ if nucleus $a$ is a hydrogen nucleus, 2 for helium, etc.), $\vec{R}_a$ is the position of nucleus $a$ in space, $\vec{r}_j$ is the position of electron $j$, and $-\frac{\hbar^2}{2m_e}\nabla_j^2$ is the kinetic energy operator for electron $j$.

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## MODELS EXPLORED

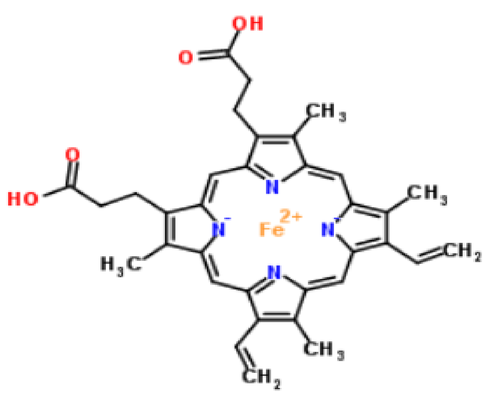
IQMOL; Q-CHEM; MAESTRO; QIKPROP, ARGUSLAB, UCSF – CHIMERA, BIOVIA DISCOVERY STUDIO - QSAR, MATERIALSTUDIO80, AVOGADRO, CHEM SPIDER MATHLAB – GRAPHICAL REPRESENTATION AND CALCULATIONS:

- Advanced molecule editor / visualizer; Designed for cross-platform use
- Molecular modeling, Bioinformatics, Materials Science, and related areas.
- Flexible high quality rendering and a powerful plugin architecture.

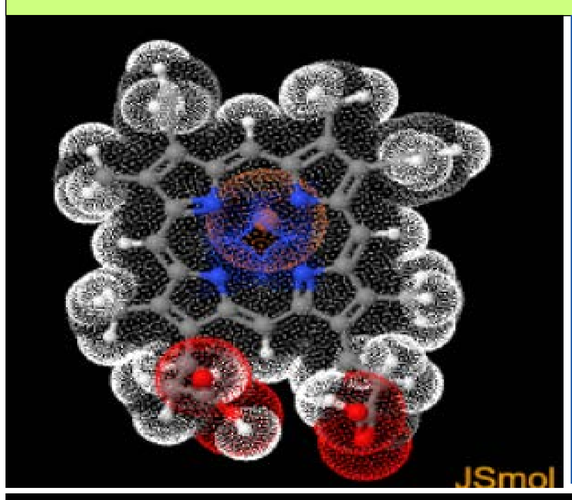
## CHIMERA MODEL OF HEMOGLOBIN

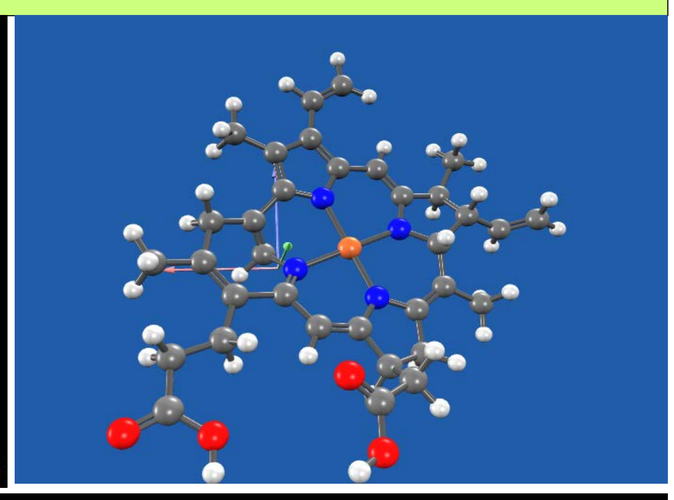
BLOOD, SPORTS, BREATHING, COMPUTERS AND CHEMISTRY

1. Open ***Chimera***; Click on > ***fetch by ID***
2. In database column click PDB and type ***1GZX***
3. At bottom of the left hand corner, click ***fetch***
4. Explore features in program (2)




## PREDICTED MODELS



There are structural relationships to compounds, functions, and reactivities. In CO poisoning the oxygen bonded to the them is displaced and held more tightly by CO. Main limitation was lack of some modeling programs.

Similar QSAR approach may be used to solve Moore's Law and the drive to develop better and low voltage devices in material science. Additional studies are needed to resolve other QSAR relationships of different classes of compounds.

## References

(1) UCB Comp. Chem Lab Book, Douskey, M; et al.
(2) www.cgl.ucsf.edu/chimera/download.html

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