

A bridge between force-field and full *ab initio* methods

Reliable prediction of thermodynamics, <sup>13</sup>C chemical shifts, solvent effects, electrostatics, and optical spectra

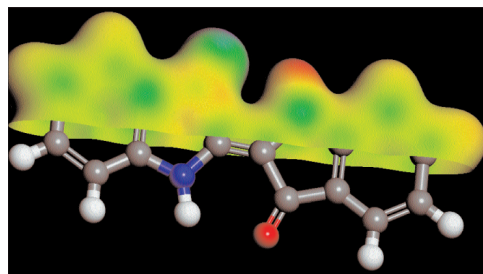
Semi-empirical program for fast geometry and transition state optimizations, and rapid access to a range of molecular properties

## VAMP

VAMP is a semi-empirical molecular orbital package for molecular organic and inorganic systems. VAMP is an ideal intermediate module between force-field and first principles methods and is capable of rapidly calculating many physical and chemical molecular properties. VAMP is optimized to be numerically stable and fast, enabling most calculations to be run interactively on a PC.

### Overview

VAMP provides fast and reliable predictions of structural and electronic properties of molecules. VAMP is an ideal choice when making tradeoffs between the speed of force-field methods and the accuracy of first-principles methods. VAMP is optimized to be numerically stable and fast, enabling user to perform high throughput calculations using even a PC.



The dye indigo showing a section of isosurface with the electrostatic potential mapped onto the electron density. Molecular electrostatic potential and total electronic density calculated using VAMP. Image generated using Materials Studio's volumetric analysis tools.

Semiempirical molecular orbital (MO) theory was developed as an everyday tool for answering questions related to standard problems in the laboratory. VAMP provides an efficient way of obtaining these results, including a simple graphical interface to make these powerful methods easily accessible. The tasks that can be performed by VAMP include geometry optimization, transition state search and optimization, and the evaluation of many chemical and physical properties.

The breadth of VAMP encompasses organic, inorganic, and organometallic molecules, polymers, oligomers, and peptides. Because of its speed, VAMP

can be used to perform scans over wide areas of a potential energy surface or reaction pathway; or it can be used to perform high-throughput calculations on hundreds or even thousands of molecules at a time. Such results can be used in conjunction with Quantitative Structure-Activity Relationships (QSAR) to create a formidable predictive tool for areas such as drug design.

VAMP contains other truly unique features that make it a powerful tool for any researcher in the chemical, pharmaceutical, or materials industry who needs to predict properties of new compounds.

For example, VAMP contains two new semi-empirical methods: MNDO/d<sup>1</sup> and AM1\*<sup>2</sup>. The latter is designed explicitly to handle transition elements, an area very challenging for semiempirical methods. The AM1\* method predicts accurate geometries and energies for metals such as Ti, Zr, and Mo. The method, in addition, increases the accuracy of results for non-transition elements such as Al, Si, and P. This is an active area of research: additional elements are provided with every new release.

VAMP is the only program that calculates both ESR hydrogen hyperfine coupling constants and <sup>13</sup>C chemical shifts. Current accuracy (standard deviations from experiment) is about 0.5 Gauss for ESR coupling constants and 6-8 ppm for <sup>13</sup>C chemical shifts<sup>3</sup>.

Solvent effects must be considered when determining the properties of molecules in almost all real situation, yet these are often ignored by calculations. Solvent effects are simulated in VAMP using two different models: numerical

Self-Consistent Reaction Field (SCRFF)<sup>4</sup> calculations, and CONductor-like Screening MOdel (COSMO)<sup>5</sup>. Such models are essential for understanding the properties of molecules in solution and are easily included in VAMP calculations.

VAMP computes optical excitation spectra (UV/vis) using the ZINDO Hamiltonians which were parameterized for this very purpose. ZINDO provides a number of different model Hamiltonians<sup>6,7</sup> that can be selected according to the desired property, accuracy, and available elements. The parameterization includes a wide number of transition metals, allowing the prediction of UV spectra for organometallic compounds as well as for organic molecules.

Electrostatic potential maps are often essential for understanding the activity of a molecule. VAMP includes routines for a rapid and accurate evaluation of the potential. The Natural Atomic Orbital-Point Charge (NAO-PC)<sup>8</sup> model is used for molecular electrostatic properties. The type of analysis obtained using NAO-PC provides a more exact picture of the molecular electronics than the normal population analysis—a picture that rivals the accuracy of ab initio methods hundreds of times slower.

Finally, VAMP provides a number of molecular properties such as ionization potential, multipole moments, accurate molecular polarizabilities, atomic polarizabilities, and optical spectra.

### ***The Materials Studio Advantage***

VAMP is operated from within the Materials Studio<sup>®</sup> software environment that provides a user-friendly interface, complying with Windows<sup>®</sup> standards. Materials Visualizer offers a wide range of model building and visualization tools that allow you to rapidly construct models of the system of interest, select the VAMP module with two mouse clicks, and run a semi-empirical calculation.

VAMP can, of course, be used to compute molecular properties as described above; or it can be used in conjunction with other modules in the Materials Studio suite of programs. VAMP predictions provide good starting points for refinement with more accurate calculations such as density functional theory (DFT). Alternatively, VAMP can compute optical & IR spectra, <sup>13</sup>C NMR shifts, or optical polarizability on molecular structures predicted by other modules of Materials Studio.

A flexible client-server architecture means that calculations can be run on Windows 2000 or XP, Linux (running on Intel 32 bit compatible systems), and IRIX servers located elsewhere on your network. Results are returned to your PC, where they may be displayed and analyzed. You can easily produce high quality graphics of molecular structures, molecular orbitals, electrostatic potentials, or charge densities. Find more information in the 'System Details' section of this document.

### ***How Does VAMP Work?***

VAMP uses semi-empirical techniques in which many of the more complex terms are ignored or replaced using approximations. Empirical parameters and functions are used to compensate for the errors introduced by these approximations. These empirical parameters are fitted to reproduce experimental data. Suitable methods for the evaluation of energetic data are MINDO/3<sup>9</sup>, MNDO<sup>10</sup>, AM1<sup>11</sup>, and PM3<sup>12</sup>. Accurate optical spectra can be obtained using the INDO<sup>6</sup> and CNDO<sup>7</sup> methods.

VAMP uses semi-empirical calculations to determine a molecular wavefunction which can then be used to derive molecular properties such as energy and dipole moments. The molecular wavefunction is constructed according to the LCAO method in which molecular orbitals are obtained as a linear combination of Slater-type atomic orbitals. Semi-empirical methods can use

Slater functions by evaluating the two-electron integrals via a multipole approximation, rather than an exact calculation.

By default, VAMP performs a MNDO Hamiltonian calculation. However, you can use controls on the VAMP setup dialog to select AM1, PM3, MNDO/C or MINDO/3 Hamiltonians. The elements for which each of these methods is parameterized are given in the 'Features and Capabilities' section of this document.

Geometry may be optimized in VAMP by several different schemes. The default optimizer is Jon Baker's Eigenvector Following (EF) routine<sup>13</sup> which was chosen for its reliability and excellent general performance. A typical geometry optimization starts either by calculating all or part of the Hessian matrix, or by estimating its diagonal values. VAMP also offers two different and very effective transition state optimizers: EF and Powell's transition state optimizer.

### Features and Capabilities

Features marked with an asterisk (\*) can not be accessed via the user interface, but are available by modifying the input file.

#### Calculation Tasks

- Open- and closed-shell Hartee-Fock methods: Restricted (RHF), Unrestricted (UHF) and spin-Annihilated Unrestricted Hartee-Fock, (A-UHF)
- Geometry optimization
- Transition state and optimization
- Vibrational frequency calculation
- Solvent effects: Self-Consistent Reaction Field (SCRf) and COnductor-like Screening MOdel (COSMO) (available solvents are acetone, acetonitrile, benzene, carbon tetrachloride, chloroform, diethyl ether, dimethyl sulfoxide, ethanol, methanol, methylene chloride, n-hexane, n-hexadecane, nitrobenzene, pyridine, water)
- CI calculations : Full, CIS, CISD and PECl

#### Hamiltonians

- MNDO [H, He, Li, Be, B, C, N, O, F, Mg, Al, Si, P, S, Cl, K, Ca, Zn, Ge, Br, Sn, I, Hg, Pb]
- MNDO/C is an MNDO method designed to be used with a perturbational theory correction for electron correlation. It is only parameterized for C, H, N and O
- AM1 [H, B, C, N, O, F, Mg, Al, Si, P, S, Cl, Zn, Ge, Br, Sn, I, Hg]
- PM3 [H, Li, Be, B, C, N, O, F, Na, Mg, Al, Si, P, S, Cl, Ca, Zn, Ga, Ge, As, Se, Br, Cd, In, Sn, Sb, Te, I, Hg, Tl, Pb, Bi]
- MNDO/d : standard MNDO parameters for : H, He, Li, Be, B, C, N, O, F, and MNDO/d parameters for: Na, Mg, Al, Si, P, S, Cl, Zn, Br, Cd, I, Hg
- AM1\* : New Hamiltonian developed for Materials Studio with standard AM1 parameters for : H, C, N, O, F and parameter sets with d-orbitals for P, S, Cl, Ti, Zr, and Mo
- CNDO/1 [H, Li, Be, B, C, N, O, F, Na, Mg, Al, Si, P, S, Cl, K, Ca, Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Br, Y, Zr, Nb, Mo, Tc, Ru, Rh, Pd, Ag, I, Lu, La, Ce, Pr, Nd, Pm, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb]
- CNDO/2 [H, Li, Be, B, C, N, O, F, Na, Mg, Al, Si, P, S, Cl, K, Ca, Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Br, Y, Zr, Nb, Mo, Tc, Ru, Rh, Pd, Ag]
- INDO/1 [H, Li, Be, B, C, N, O, F, Na, Mg, Al, Si, P, S, Cl, K, Ca, Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Br, Y, Zr, Nb, Mo, Tc, Ru, Rh, Pd, Ag, I]
- INDO/2 [H, Li, Be, B, C, N, O, F, Na, Mg, Al, Si, P, S, Cl, K, Ca, Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Br]

#### Job Control Options

- VAMP jobs can be run as background processes on a server or as synchronous (interactive) jobs on your PC.

## Features and Capabilities (Continued)

### Properties

- Electron density
- Molecular orbitals (canonical), or localized orbitals
- Electrostatic potentials
- Atomic charges : NAO-PC, Coulson, and Mulliken
- Molecular and atomic multipoles
- Static first-order polarizabilities(\*)
- ESR hyperfine coupling constants to hydrogen(\*)
- <sup>13</sup>C chemical shifts
- Optical spectra
- Heat of formation, entropy, and heat capacity.

### Analysis of VAMP results

- Volumetric display of: total electronic density, spin density, electrostatic potential, molecular orbitals, and localized orbitals
- Thermodynamic properties (enthalpy, entropy, and heat capacity)
- Atomic charges and bond orders.

### System Requirements:

For Materials Studio system requirements see [www.accelrys.com/products/mstudio/sysreqs.html](http://www.accelrys.com/products/mstudio/sysreqs.html)

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