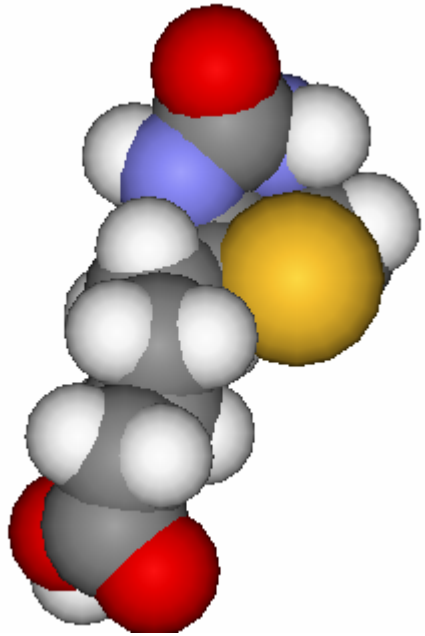
What Can DS ViewerPro Do For Me ?



S. Ravichandran, Ph.D.

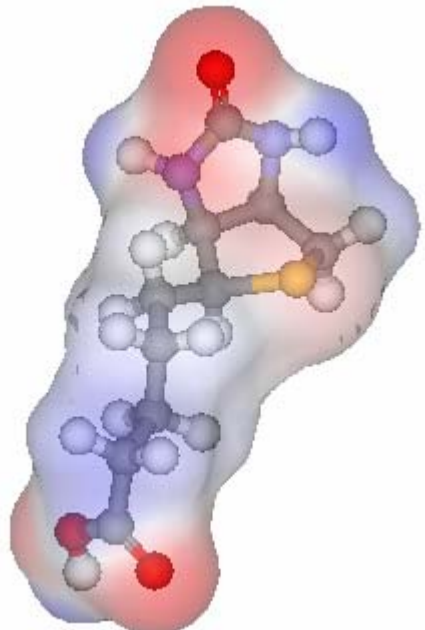
http://ncisgi.ncifcrf.gov/~ravichas/MM/MM.htm

ABCC

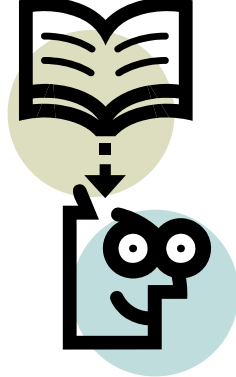
NCI-Frederick

MD 21702

June 08, 2005



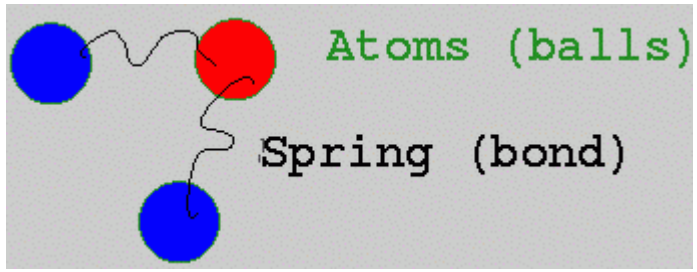
Help



- Manuals for DS ViewerPro
  - Conformer, Molecular Overlay & Property Calculator
- Manuals are available locally for browsing
  - Option for searching words/terms in the manual
- Option to convert manuals as PDF files for saving and printing

Basic Assumptions Behind DS ViewerPro

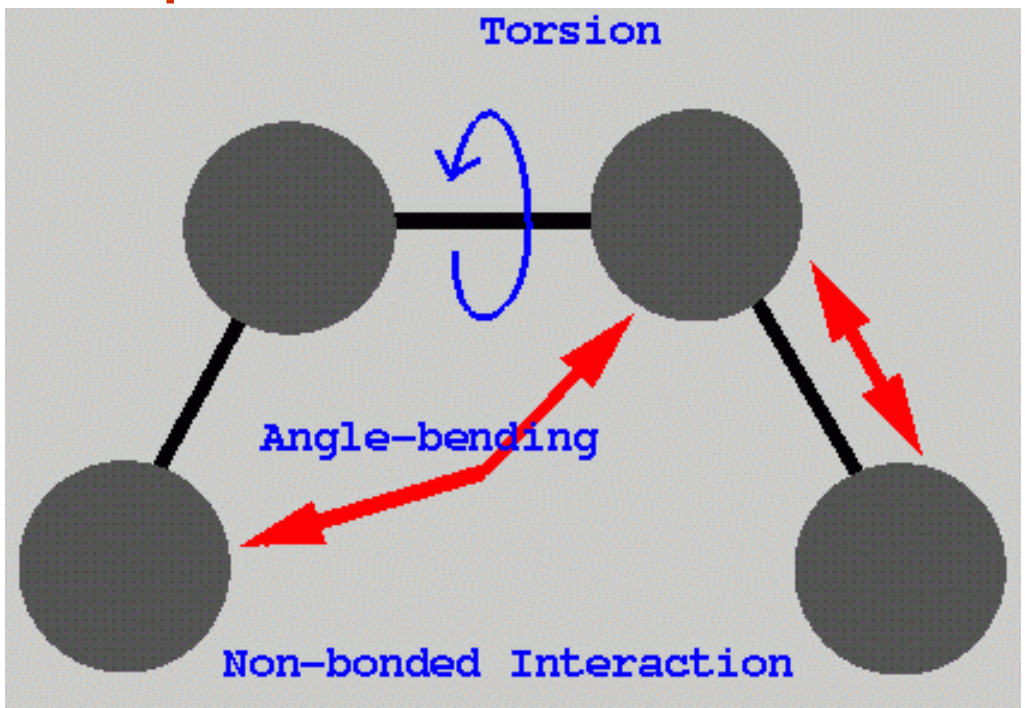
Clean Structure



- Electrons and nuclei are lumped together
  - Born-Oppenheimer Approximation
    - Separation of electron (e^-) movement (fast) from the slow nuclei (X)
- Molecules are assumed to be soft balls (point masses) and connected to others by bonds (springs)
- Total energy of the system is an important property and it is usually computed as a sum of independent energy terms.

ForceField

- ForceField is an analytical Functional form for the independent energy terms and parameters



$$E_{pot} = \boxed{\Sigma 1/2K_b(b - b_0)^2} + \Sigma 1/2K_\theta(\theta - \theta_0)^2 + \Sigma 1/2K_\phi(1 + \mathrm{Cos}N\phi)^2 + \Sigma 1/2K_\chi(\chi - \chi_0)^2 \; \Sigma((B/r)^{12} - (A/r)^6) + \Sigma(qq/r)$$

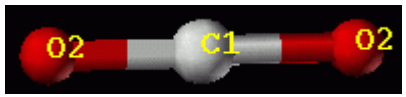
VDW

electrostatic

Bond Stretching = $K(b-b_0)^2$
Simple Functional Form

Hooke's Law

Energy Minimization



- Each atom/bond in a molecule or amino acid is identified by
  - 1) Atom type 2) Residue type 3) hybridization type 4) Bonding info. 5) Charges 6) Coordinates

Carbon-di-oxide

- Atom types C1, O2; Hybridization: sp, sp2; Bonding info: C1 is bonded to two O2 atoms; Coordinates: x,y and z; Charges: (C) 0.372, (O) -0.186

DS ViewerPro: More than a viewer

- Forcefield: Dreiding Forcefield
  - Simple forcefield

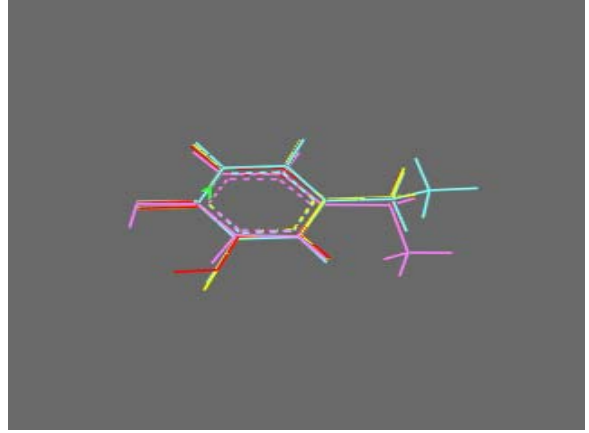
    May, S.L.; Olafson, B.D.; Goddard, W.A. Journal of Physical Chemistry, 1990, 94(26), 8897-8909

    - Force constants and geometry parameters for single atoms (unlike other forcefields which has parameters for combination of atoms)
    - Moderate coverage of periodic table
  - VDW (Lennard-Jones), electrostatic (distance-dependent dielectric function), H-bond (12-10)
  - Energy minimization is done using steepest descent

Property Calculator

- AlogP 98
- Jurs Polar Surface Area Descriptors
  - PPSA-1, PNSA-1 etc.
    - Partial Positive Surface Area (PPSA)
- Rule of Five
  - Lipinksi violations
    - More than 5 HBD, MWT > 500, LopP is over 5, more than 10 HBA
- Dipole moment, Molecular Density
- Number of HBAs, HBDs, Rotatable bonds, Chiral centers
- Polarizability, Radius of gyration, Sum of formal charges, Sum of partial charges, Surface Area

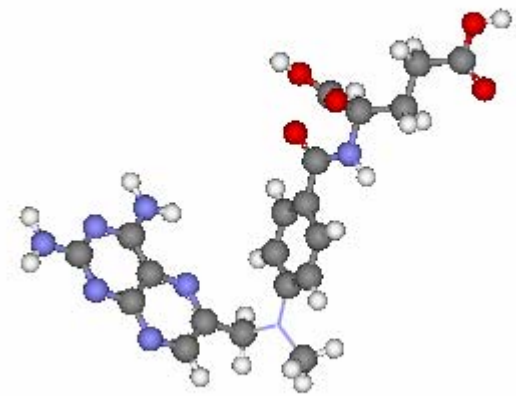
Align/Overlay small molecules



- Align
  - Create tethers on corresponding atoms in the molecules-Align
    - Align will do a rigid body superposition
      - First chosen molecule will be reference
      - Results will be reported as Root Mean Square Displacement (RMSD)
- Overlay
  - Using Fit (RMSD) or Field (electrostatic + vdw) options
  - Targeted (Specify a target and to which all others are aligned) or consensus (best average overlay)

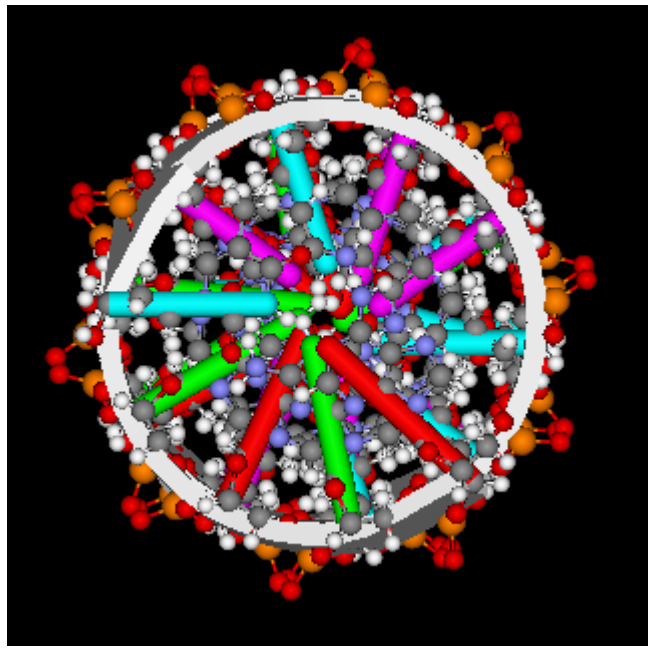
Small Molecules

- Save the data, save the picture
  - ***MSV, PDB,ENT, mol, sd, sdf, mdl. CAR, mol2, msf, msi, CIF, xyz, skl, smi, grd…….***
  - ISISDRAW, ChemDraw, **ChemSketch**
    - Drag and Drop, 2D -> 3D
  - SMILES string
  - Sketch them
- Ability to read multiple molecules
  - Align/overlay molecules
- Display labels, Change display types
- Minimize clean up
- Calculate properties
- Save the data, save the picture



Biomolecules Proteins/DNA/RNA

- How to read a locally stored PDB file?
- How to download them directly from RCSB or any other computer/location
  - X-ray, NMR
- How to explore structural – information ? Display Properties
  - Amino acids, atom types
  - Secondary Structure prediction
    - Kabsch & Sander
  - Hydrophobicity
    - Kyte-Doolittle
  - Hierarchy view
- How to print or save them ?



Other features

- Crystal viewer
- Scripting
- Customizing features
  - Visual Basic and Visual C++

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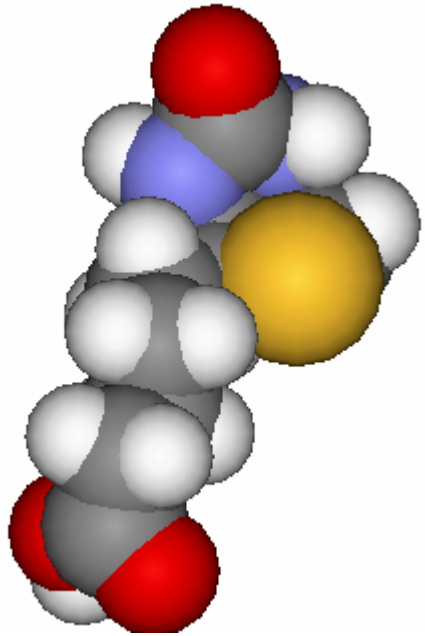
What can DS ViewerPro Do For Me ?

Hands-on Exercises



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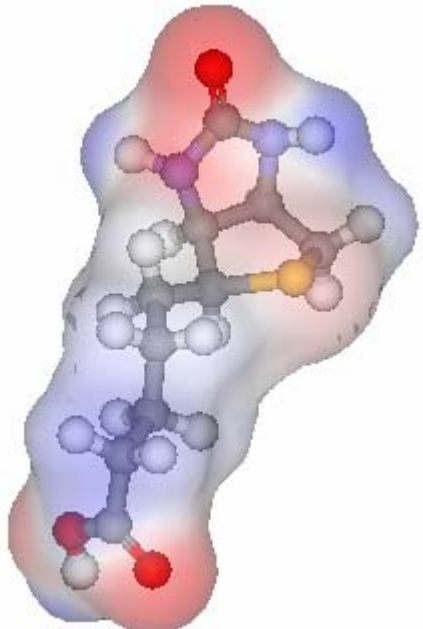
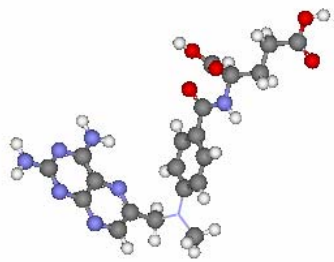
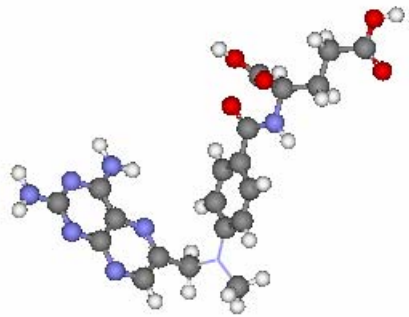


Hands-on: Small Molecules



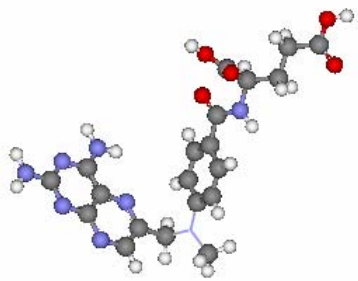
- Exercise 1: Introduction to Help menu
- Exercise 2: Reading small molecules (Sybyl and Catalyst formats)
  - Use '*Biotin.mol2', 'MethotrexateCPD'* for this exercise
  - What other formats DSV can handle?
    - Exercise 2a: For handling SD files, use 'MethotrexateSD.sd'. Also try Animate option for this exercise.
- Exercise 3: Input a SMILES string and demonstrate that the DS ViewerPro can interpret it and automatically convert the 2D information to 3D
    - Input 'Aspirin.smi' to read in the SMILES string for Aspirin
  - How to import molecules (2D) from ChemSketch (ChemSketch is an external application, and has to be installed prior to this exercise)
    - Double-click 'terpinoid.skd' to open Terpinoid in ChemSketch. Do a Control-C and paste it in DSViewerPro.

Hands-on: Small Molecules



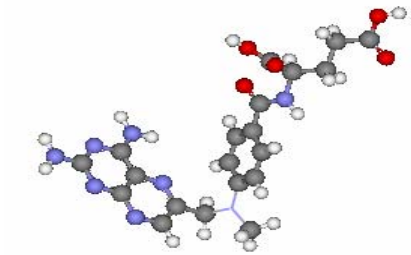
- Exercise 4: Demonstrate how to sketch molecules in DS ViewerPro
- Exercise 5: How to read more than one molecule?
  - How to read more than one molecule in the same window ?
- Exercise 6: DS ViewerPro view of small molecules
  - Relation between Hierarchy window and 3D window

Hands-on: Small Molecules



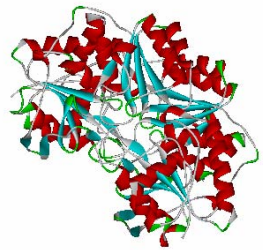
- Exercise 7: How to display -2D and -3D views of the molecule at the same time?
  - Use ‘Biotin.mol2’ for this exercise
- Exercise 8: How to display labels (name, charges, chirality etc)?
  - How to change display style (ball-stick, space-fill etc.)?
- Exercise 9: Read ‘Aspirin.smi’, calculate charge, display charges, display Dreiding parameters and perform an energy minimization.

Hands-on: Small Molecules



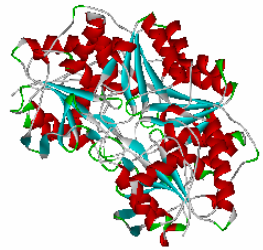
- Exercise 10:How to calculate important small molecule properties? How to display and export them to MS Office software (ex Excel etc.) ?
- Exercise 11: How to align/overlay small molecules ?
  - Use ‘alignex.msv’ for this exercise

Hands-on: Biomolecules



- Exercise 1: Load a X-ray PDB file
  - Read a PDB file and explore the structure
    - Use PDB ID ‘1wsa.pdb’ for this exercise
- Exercise 2: Load an NMR file from PDB
  - Use 1dv0.msv for this exercise
    - Do you see all the models?
      - Tools → Animation → Add
      - View → Animate
- Exercise 3: Load a DNA molecule
  - Use ‘DNA.msv’ for this exercise
- Exercise 4: Explore Display style, surface, labels and Hierarchy View

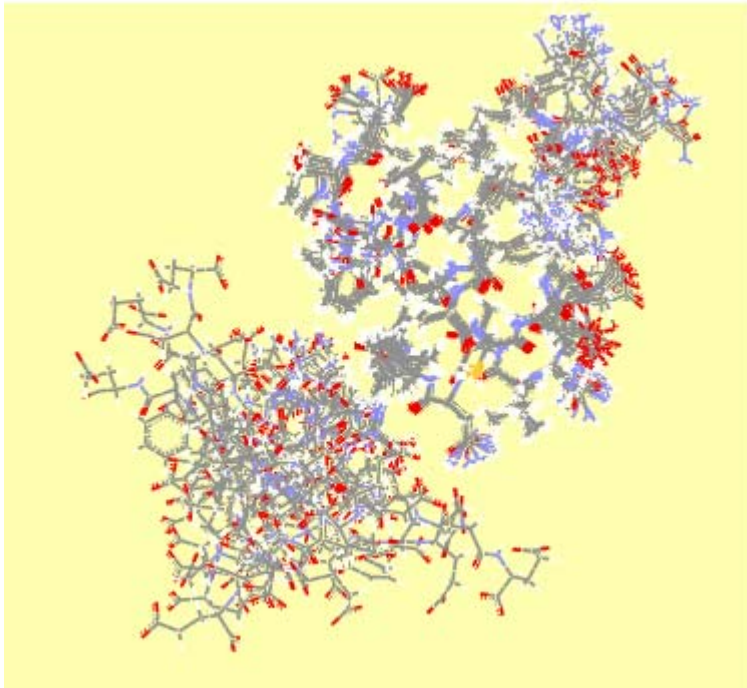
Hands-on: Biomolecules



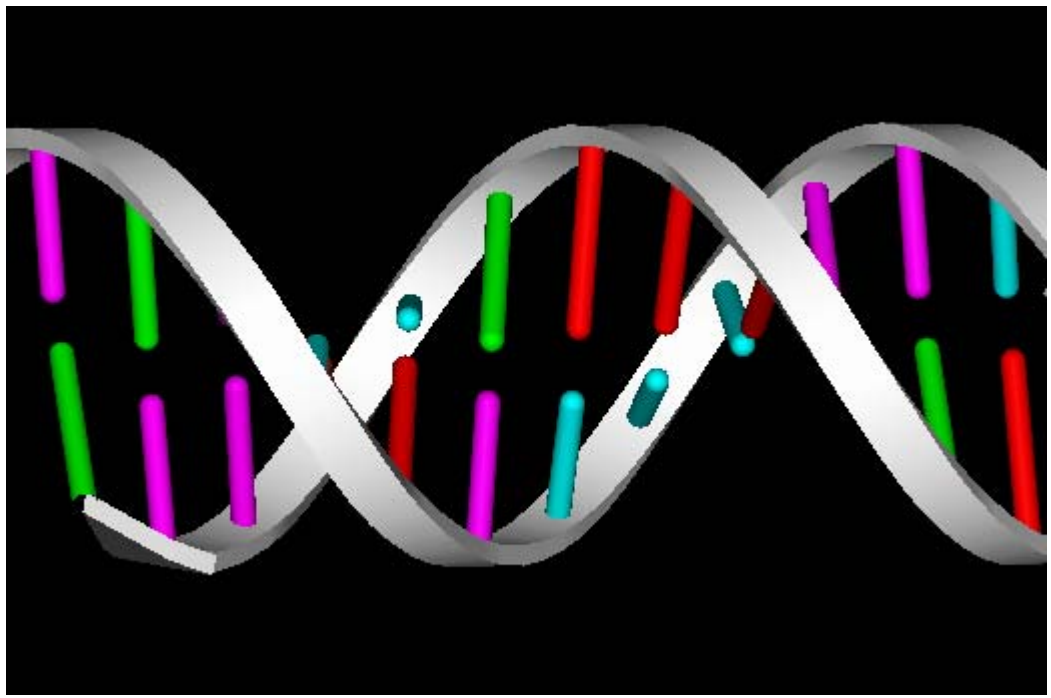
- Exercise 5: Read a structure and check its validity
  - Tools > Monitor > Structure
  - Use '1wsa.pdb' for this exercise
- Exercise 6: Exploring the active site of 1STP.
  - File → Open → '1STP.pdb ' Then, Tools → Hydrogens→ Add
  - Open 'Hierarchy window', zoom-in and manually select the ligand (Double Left-Click on any atom of the ligand) only and go to
    - Edit → Group →'Ligand' and hit 'Define', then
    - Edit → Select All, then, View → Hide, then
    - Use Hierarchy window to select 'Ligand' group we created
    - Edit → 'Select…' → Type (AminoAcid) & Radius '5.0' and hit 'Select',
    - View → 'Show only', then unselect everything, Tools → Monitor → Hbond, select Ligand only and create a solvent accessible surface by going to Tools → Surfaces → Add

Hands-on: General Options

- View -> Options
  - To change selection tools
    - View -> options -> Tools
- How to print from DS-Viewer Pro ?
- How to export molecules from DS ViewerPro to other windows appli-cation such as powerpoint, word etc. ?
  - How to share results (figures) with students/collaborators?



Gif figure not DS ViewerPro molecule

ActiveX Tutorial

- DNA.msv