APBS-PDB2PQR Documentation

Release 1.6

Nathan Baker

Jul 05, 2017

Contents:

APBS (Adaptive Poisson-Boltzmann Solver) and PDB2PQR are software packages designed to analyze the solvation properties of small molecules as well as macro-molecules such as proteins, nucleic acids, and other complex systems. This is the documentation for these packages; more information can be found at the APBS-PDB2PQR homepage.

CHAPTER 1

APBS-PDB2PQR overview

Why APBS and PDB2PQR?

An understating of electrostatic interactions is essential for the study of bio-molecular processes. The structures of proteins and other bio-polymers are being determined at an increasing rate through structural genomics and other efforts while specific linkages of these biopolymers in cellular pathways or supramolecular assemblages are being detected by genetic and proteomic studies. To integrate this information in physical models for drug discovery or other applications requires the ability to evaluate the energetic interactions within and between bio-polymers. Among the various components of molecular energetics, solvation properties and electrostatic interactions are of special importance due to the long range of these interactions and the substantial charges of typical biopolymer components.

APBS is a unique software which solves the equations of continuum electrostatics for large biomolecular assemblages. This software was designed "from the ground up" using modern design principles to ensure its ability to interface with other computational packages and evolve as methods and applications change over time. The APBS code is accompanied by extensive documentation for both users and programmers and is supported by a variety of utilities for preparing calculations and analyzing results. Finally, the free, open-source APBS license ensures its accessibility to the entire biomedical community.

The use of continuum solvation methods such as APBS requires accurate and complete structural data as well as force field parameters such as atomic charges and radii. Unfortunately, the limiting step in continuum electrostatics calculations is often the addition of missing atomic coordinates to molecular structures from the Protein Data Bank and the assignment of parameters to these structures. To adds this problem, we have developed PDB2PQR. This software automates many of the common tasks of preparing structures for continuum solvation calculations as well as many other types of biomolecular structure modeling, analysis, and simulation. These tasks include:

- Adding a limited number of missing heavy (non-hydrogen) atoms to biomolecular structures.
- Estimating titration states and protonating biomolecules in a manner consistent with favorable hydrogen bonding.
- Assigning charge and radius parameters from a variety of force fields.
- Generating "PQR" output compatible with several popular computational modeling and analysis packages.

This service is intended to facilitate the setup and execution of electrostatics calculations for both experts and non-experts and thereby broaden the accessibility of biomolecular solvation and electrostatics analyses to the biomedical

community.

Both APBS and PDB2PQR have enjoyed widespread adoption throughout the biomedical community and are used in numerous applications involving biomolecular structures.

What do I do next?

1. **Before you start**, please make sure to support the APBS/PDB2PQR team by registering your use of the software.
2. **Download the software** following the instructions at *How to get the software*.

If you come across anything along the way that we haven't covered, is incorrect information, or if you know of a tip you think others would find useful, please let us know (see *Getting help*) and we'll work on including it in this guide.

CHAPTER 2

How to get the software

Before you begin! APBS-PDB2PQR funding is dependent on your support for continued development and support. Please register before using the software so we can accurately report the number of users to our funding agencies.

Web servers

Most APBS and PDB2PQR functionality is available through our online web servers. However, if you prefer to download the software, *skip to the downloads section*.

The PDB2PQR web server offers a simple way to use both APBS and PDB2PQR without the need to download and install additional programs.

The PDB2PQR web server is hosted by the National Biomedical Computation Resource. Please visit http://nbcr-222.ucsd.edu/pdb2pqr to access the web server.

Downloads

If you prefer to download the software rather than use the APBS webserver, both APBS and PDB2PQR are also available for download to use in standalone mode. Users can either download binaries for their platform or compile the software from source (GitHub)

APBS downloads

Both binary executables and source code are available for APBS. The best way to acquire APBS is to register, which helps us track usage of the software for our funding agencies, and then download the software from SourceForge (APBS).

If you download the *developmental* source code version of APBS from GitHub, please follow the compilation and installation instructions provided with the source code.

Usage information for APBS is available at *APBS*.

PDB2PQR downloads

PDB2PQR is currently available in source code form. Stable versions can be downloaded from *SourceForge (PDB2PQR)* and developmental versions can be checked out from GitHub. If you are installing from source, please follow the instructions at *Installing PDB2PQR*. After compilation, PDB2PQR can be used as described at *PDB2PQR*.

Release histories

APBS 0.1.0 (2001-08)

I am pleased to announce the availability of a pre-beta version of the Adaptive Poisson-Boltzmann Solver (APBS) code to selected research groups. APBS is new software designed to solve the Poisson-Boltzmann equation for very large biomolecular systems. For more information, please visit the APBS web site at http://mccammon.ucsd.edu/apbs.

This release is designed to allow interested users to get familiar with the code. It is not currently fully functional; it only provides for the sequential multigrid (Cartesian mesh) solution of the linearized and nonlinear Poisson-Boltzmann equation. User-friendly parallel support will be incorporated into the next release. Other limitations that may impact its immediate usefulness are:

- No finite element support. This is awaiting the public release of the Holst group's FEtk library.
- Somewhat inefficient coefficient evaluation (i.e., problem setup). This should be fixed in the next release or two.

Rather than serving as a production code, this release represents a request for help in breaking the software and finding its deficiencies before a public beta.

If you are interested in testing this early release, please go to http://wasabi.ucsd.edu/~nbaker/apbs/download/. Since this is not a public release of APBS, you will need to enter the user-name "apbs-beta" and the password "q94p$fa!" for access to this site. Once there, please follow the instructions to download and install APBS.

If you are not interested in trying out this early release, but would like to stay informed about subsequent versions of APBS, please consider subscribing to the APBS announcements mailing list by sending the message "subscribe apbs-announce" to majordomo@mccammon.ucsd.edu.

Thank you for your time and interest in the APBS software.

APBS 0.1.1 (2001-08)

I am slightly less pleased to announce the first bug-fix for APBS, version 0.1.1. This fixes compilation problems that popped up for several folks, including:

- Syntax errors with non-GNU compilers
- Errors in the installation instructions
- Installation of binary in machine-specific directory

APBS 0.1.2 (2001-09)

This version is mainly designed to increase portability by switching to libtool for library creation and linking. Of course, it also contains a few bug fixes. Highlights include:

- Changes to the User Manual
- Addition of a Programmer's Manual
- Various FEtk-related things (no particular impact to the user)

- Improvements to the test systems
- Change in the format for printing energies
- Change in directory structure
- Fixed centering bug in main driver (only impacted I/o)
- Fixed error message bug in VPMG class
- Fixed grid length bug (popped up during sanity checks) in VPMG class
- Switched to libtool for linking
- Note that Compaq Tru64 Alpha users may still experience problems while compiling due to some strangess with linking C and FORTRAN objects.

APBS 0.1.3 (2001-09)

This version features a few improvements in scripts, PDB parsing flexibility, and portability, including:

- Dave Sept upgraded the psize and shift scripts to allow more flexibility in PDB formats.
- Chain ID support has been added to the PDB/PQR parser
- Removed -g from compiler flags during linking of C and FORTAN under OSF (thanks to Dagmar Floeck and Julie Mitchell for help debugging this problem)

APBS 0.1.4 (2001-09)

This version features major bug fixes introduced in the 0.1.3 release:

- Chain ID support has been **removed** from the PDB/PQR parser (if anyone has a nice, flexible PDB parser they'd like to contribute to the code, I'd appreciate it)
- Configure script has been made compatible with OSF
- Bug fix in disabling FEtk-specific header files

APBS 0.1.5 (2001-10)

This version features minor bug fixes and several new features:

- Fixed shift in center of geometry for OpenDX I/O
- Made energy evaluation more robust when using NPBE
- Rearrangments of files and modified compilation behavior
- Input file support for ion species of varying valency and concentration
- Input file support incorrect nlev/dime combinations; APBS now finds acceptable settings near to the user's requested values
- "Automatic focusing". Users now simply specify the physical parameters (temperature, dielectric, etc.), the coarse and fine grid lengths and centers, and APBS calculates the rest

APBS 0.1.6 (2001-11)

This version is a public (beta) release candidate and includes the following bug-fixes and features:

- Fixed printf formatting in UHBD potential output
- Added input file support for parallel focusing
- Fixed small bug in parsing writeacc syntax (thanks, Dave)
- Added output file support for parallel focusing
- Changed some documentation

You need to download a new version of MALOC for this release.

APBS 0.1.8 (2002-01)

This version is a public (beta) release candidate and includes the following bug-fixes:

- Added warning to parallel focusing
- Added several test cases and validated the current version of the code for all but one (see examples/README.html)
- Fixed atom partitioning bug and external energy evaluation during focusing
- Added new program for converting OpenDX format files to MOLMOL (by Jung-Hsin Lin)

You should definitely upgrade, the previous versions may produce unreliable results.

APBS 0.2.0 (2002-03)

This version is a public (beta) release candidate and includes:

- Slight modification of the user and programmer's guides
- Scripts for visualization of potential results in VMD (Contributed by Dave Sept)
- Corrections to some of the example input files
- A few additional API features

This release requires a new version of MALOC.

APBS 0.2.1 (2002-04)

This version requires the latest version of MALOC to work properly!

- Syntax changes
  - The writepot and writeacc keywords have been generalized and new I/O features have been added. The syntax is now:
    - write pot dx potential
    - write smol dx surface
    - etc. Please see the User's Manual for more information

  - The read keywords has been generalized and new I/O features have been added which support the use of pre-calculated coefficient grids, etc. The correct syntax for reading in a molecule is now "read mol pqr mol.pqr end"; please see the User's Manual for more information.
  - The "mg" keyword is no longer supported; all input files should use "mg-manual" or one of the other alternatives instead.
- A change in the behavior of the "calcenergy" keyword; passing an argument of 2 to this keyword now prints out per-atom energies in addition to the energy component information
- A new option has been added to tools/manip/acc to give per-atom solvent-accessible surface area contributions
- A new option has been added to tools/manip/coulomb to give per-atom electrostatic energies
- Added tools/mesh/dxmath for performing arithmetic on grid-based data (i.e., adding potential results from two calculations, etc.)
- Added tools/mesh/uhbd_asc2bin for converting UHBD-format grid files from ASCII to binary (contributed by Dave Sept)
- Improvement of VMD visualization scripts (contributed by Dave Sept)
- The API has changed significantly; please see the Programmer's Manual.
- Working (but still experimental) Python wrappers for major APBS functions.
- More flexible installation capabilities (pointed out by Steve Bond)
- Added ability to use vendor-supplied BLAS
- Brought up-to-date with new MALOC

APBS 0.2.2 (2002-08)

- There were several other changes along the way... I lost track.
- Changed coordinate indexing in some energy calculations
- Updated documentation to reflect recent changes on Blue Horizon
- Improved speed of problem setup BUT NOW RESTRICT use of input coefficient maps (see documentation)
- Updated documentation, placing particular emphasis on use of Intel compilers and vendor BLAS on Intel Linux systems
- Fixed bug for nonpolar force evaluation in Vpmg_dbnpForce
- Removed MG test scripts; use `bin/*.c` for templates/testing
- Made main driver code completely memory-leak free (i.e., if you wanted to wrap it and call it repeatedly – Thanks to Robert Konecny)
- Fixed main driver code for compatibility with SGI compilers (Thanks to Fabrice Leclerc)
- Made focused evaluation of forces more sensible.
- Added 'print force' statement
- Fixed bug in OpenDX input/output (OpenDX documentation is lousy!)

APBS 0.2.3 (2002-10)

- Fixed bugs in salt-dependent Helmholtz/nonlinear term of PBE affecting both LPBE and NPBE calculations. While this bug fix only changes most energies by < 2 kJ/mol, it is recommended that all users upgrade. Many thanks to Michael Grabe for finding and carefully documenting this bug!
- A parameter (chgm) has been added which controls the charge discretization method used. Therefore, this version contains substantial changes in both the API and input file syntax. Specifically:
  - PBEparm has two new members (chgm, setchgm)
  - Vpmg_fillco requires another argument
  - Vpmg_*Force functions require additional arguments
  - Input files must now contain the keyword "chgm #" where # is an integer
  - Please see the documentation for more information.
- Fixed problems with "slicing" off chunks of the mesh during I/O of focused calculations
- Updated authors list
- New CHARMM parameters – Robert Konecny
- Created enumerations for common surface and charge discretization methods
- Added Vmgrid class to support easy manipulation of nested grid data
- Added more verbosity to error with NPBE forces
- Added working Python wrappers – Todd Dolinksy
- Modified VMD scripts read_dx and loadstuff.vmd

APBS 0.2.4 (2002-10)

- Fixed bug which set one of the z-boundaries to zero for "bcfl 1". This can perturb results for systems where the grid boundaries are particularly close to the biomolecule. While this is an embarassing bug, most systems using settings suggested by the psize script appear largely unaffected (see examples/README.html). Thanks to Michael Grabe for finding this bug (Michael, you can stop finding bugs now...)
- Updated VMD scripts to agree with the current OpenDX output format
- A COMMENT: As far as I can tell, the current version of OpenDX-formatted output (same as version 0.2.3) is fully compliant with the OpenDX standards (see, for example, http://opendx.npaci.edu/docs/html/pages/usrgu065.htm#HDRXMPLES). However, I realize this is different than the format for previous versions and would encourage all users to update their APBS-based applications to accomodate these changes. The best solution would be for all downstream applications to use the APBS Vgrid class (see http://agave.wustl.edu/apbs/doc/api/html/group__Vgrid.html) to manipulate the data since this class should remain internally consistent between releases. Finally, I would love to have some OpenDX guru who uses APBS to contact me so I can solidfy the data ouput format of APBS. I'm about ready to permanently switch to another format if I can't reach a consensus withOpenDX...

APBS 0.2.5 (2002-11)

- Improved consistency between energies evaluated with "chgm 0" and "chgm 1"
- Made charge-field energy evaluation consistent for user-supplied charge maps
- Added new psize.py script courtesy of Todd Dolinsky.

- Updated list of APBS-related tools in User Guide.
- Added RPM capabilities courtesy of Steve Bond.
- Removed annoying excess verbosity from Vgrid.
- Updated Blue Horizon compilation instructions (thanks to Robert Konecny and Giri Chukkapalli)
- Updated autoconf/automake/libtool setup and added –disable-tools option

APBS 0.2.6 (2003-01)

- Changed license to GPL
- Made a few routines compliant with ANSI X3.159-1989 by removing snprintf (compliant with ISO/IEC 9899:1999). This is basically for the sake of OSF support.

APBS 0.3.0 (2004-02)

News

APBS is now supported by the NIH via NIGMS grant GM69702-01.

Changes that affect users

- New version of the documentation
- New directory structure in tools/
- Finished fe-manual mode for ELEC calculations – this is the adaptive finite element solver
- Added documetnation for fe-manual
- New apbs/tools/manip/inputgen.py script to automatically generate input APBS files from PQR data
- Added new asynchronous mode in mg-para parallel calculations to enable running on-demand and/or limited resources
- Added new script (tools/manip/async.sh) to convert mg-para calculations in mg-async calculations
- Added following aliases for some of the more obscure parameters in the input files:
- chgm 0 ==> chgm spl0
- chgm 1 ==> chgm spl2
- srfm 0 ==> srfm mol
- srfm 1 ==> srfm smol
- srfm 2 ==> srfm spl2
- bcfl 0 ==> bcfl zero
- bcfl 1 ==> bcfl sdh
- bcfl 2 ==> bcfl mdh
- bcfl 4 ==> bcfl focus
- calcenergy 0 ==> calcenergy no
- calcenergy 1 ==> calcenergy total

- calcenergy 2 ==> calcenergy comps
- calcforce 0 ==> calcforce no
- calcforce 1 ==> calcforce total
- calcforce 2 ==> calcforce comps
- Example input files have been updated to reflect this change. NOTE: the code is backward-compliant; i.e., old input files WILL still work.
- Added new READ options "PARM" and "MOL PDB", see documentation for more information. These options allow users to use unparameterized PDB files together with a parameter database.
- Updated the documentation
- Now include support for chain IDs and other optional fields in PQR/PDB files
- Added support for parsing PDB files
- Renamed:
- amber2charmm -> amber2charmm.sh
- pdb2pqr -> pdb2pqr.awk
- qcd2pqr -> qcd2pqr.awk
- Added a new Python-based pdb2pqr (tools/conversion/pdb2pqr) script that allows users to choose parameters from different forcefields.
- Updated Python wrappers (tools/python) and added the python directory to autoconf/automake.
- Reformatted examples/README.html for readability.

Bug fixes

- Fixed bug in PQR parsing that can cause PDB/PQR files to be mis-read when they contain residues with numbers in their names (Thanks to Robert Konecny and Joanna Trylska)
- Fixed bug when writing out number/charge density: unrealistic densities reported inside iVdW surface.
- Fixed bug in VMD read_dx utility
- Invalid map IDs now result in an error message instead of a core dump (thanks to Marco Berrera)
- Modified mechanism for cubic-spline output, fixing a bug associated with zero-radius atoms
- Fixed omission of srfm in sections of documentation (thanks to Sameer Varma)
- Made autoconf/automake configure setup more robust on Solaris 8 platforms (thanks to Ben Carrington)

Changes that affect developers

- New docuemtnation setup
- New tools/ directory structure
- Changed Vgreen interface and improved efficiency
- Changed Vopot interface to support multiple grids
- Added several norm and seminorm functions to Vgrid class
- Altered –with-blas syntax in configure scripts and removed –disable-blas

- Documented high-level frontend routines
- Cool new class and header-file dependency graphs courtesy of Doxygen and Graphviz
- Added substantial mypde.c-based functionality to Vfetk
- Moved chgm from PBEparm to MGparm
- Minor changes to Vfetk: removed genIcos and added genCube
- FEM solution of RPBE working again (see test/reg-fem) and is probably more up-to-date than test/fem
- Updated API documentation
- Changed many NOsh, FEMparm, MGparm variables to enums
- Changes to Valist and Vatom classes
- Fixed minor bugs in documentation formatting
- Made Vopot more robust
- Created Vparam class for parameter file parsing
- Added vparam* parameter database flat files to tools/conversion/param

APBS 0.3.1 (2004-04)

New features

- New APBS tutorial
- New `tools/python/vgrid/mergedx.py` script to merge dx files generated from parallel APBS runs back into a single dx file.

Bug fixes

- Fixed bug in parallel calculations where atoms or points on a border between two processors were not included. Modified setup algorithm for parallel calculations to allow partitions in order to obtain grid points and spacing from the global grid information.
- Modified extEnergy function to work with parallel calculations, giving better accuracy.

APBS 0.3.2 (2004-11)

New features

- Updated tutorial with more mg-auto examples
- Updated apbs.spec file for generating RPMs on more platforms.
- Added new Python wrapper to tools/python directory showing how to run APBS without PQR and .in inputs.
- Python wrappers are now configured to compile on more architectures/ from more compilers.
- Updated tools/conversion/pdb2pqr to a new version (0.1.0) of PDB2PQR, which now can handle nucleic acids, rebuild missing heavy atoms, add hydrogens, and perform some optimization.

Bug fixes

- The dimensions of the fine grids in the pka-lig example calculations were increased to give more reliable results (albeit ones which don't agree with the reported UHBD values as well).
- hz in mgparse.c causes name clash with AIX environmental variable; fixed.
- Fixed documentation to state that using a kappa map does not ignore ELEC ION statements.
- Added a stability fix for printing charge densities for LPBE-type calculations.
- Fixed a bug in NPBE calculations which led to incorrect charge densities and slightly modified total energies.
- Modified the origin when creating UHBD grids to match standard UHBD format.
- Fixed VASSERT error caused by rounding error when reading in dx grid files.

PDB2PQR 1.0.0 (2005-08)

This is the initial version of the PDB2PQR conversion utility. There are several changes to the various "non-official" versions previously available:

- SourceForge has been chosen as a centralized location for all things related to PDB2PQR, including downloads, mailing lists, and bug reports.
- Several additions to the code have been made, including pKa support via PropKa, a new hydrogen optimization algorithm which should increase both accuracy and speed, and general bug fixes.

PDB2PQR 1.0.1 (2005-10)

New features

- Added citation information to PQR output.

Bug fixes

- Fixed a bug during hydrogen optimization that left out H2 from water if the oxygen in question had already made 3 hydrogen bonds.

APBS 0.4.0 (2005-12)

New features

- New version of the 'acc' program available.
- Added additional verbosity to APBS output.
- Added tools/python/vgrid to the autoconf script. The directory compiles with the rest of the Python utilities and is used for manipulating dx files.
- Modified the tools/python/noinput.py example to show the ability to get and print energy and force vectors directly into Python arrays.
- Added dx2uhbd tool to tools/mesh for converting from dx format to UHBD format (Thanks to Robert Konecny)
- Added ability of tools/manip/inputgen.py to split a single mg-para APBS input file into multiple asynchronous input files.

- Modified inputgen.py to be more flexible for developers wishing to directly interface with APBS.
- Added Vclist cell list class to replace internal hash table in Vacc
- Modified Vacc class to use Vclist, including changes to the Vacc interface (and required changes throughout the code)
- Consolidated Vpmg_ctor and Vpmg_ctorFocus into Vpmg_ctor
- Consolidated vpmg.c, vpmg-force.c, vpmg-energy.c, vpmg-setup.c
- Added autoconf support for compilation on the MinGW32 Windows Environment
- Added autoconf support (with Python) for Mac OS 10.4 (Tiger)
- Added the function Vpmg_solveLaplace to solve homogeneous versions of Poisson's equation using Laplacian eigenfunctions.
- Modified the dielectric smoothing algorithm (srfm smol) to a 9 point method based on Bruccoleri, et al. J Comput Chem 18 268-276 (1997). NOTE: This is a faster and more flexible smoothing method. However, when combined with the the molecular surface bugfixes listed below, this change has the potential to make the srfm smol method give very different results from what was calculated in APBS 0.3.2. Users who need backwards compatibility are encouraged to use the spline based smoothing method (srfm spl2) or the molecular surface without smoothing (srfm mol).
- Added new 'sdens' input keyword to allow user to control the sphere density used in Vacc. This became necessary due to the Vacc_molAcc bug fix listed below. Only applies to srfm mol and srfm smol.
- Made the examples directory documentation much more streamlined.
- Added tests for examples directory. Users can now issue a "make test" in the desired directory to compare local results with expected results. Also includes timing results for tests for comparison between installations.

Bug fixes

- Fixed a bug in Vpmg_qmEnergy to remove a spurious coefficient of z_i^2 from the energy calculation. This generated incorrect results for multivalent ions (but then again, the validity of the NPBE is questionable for multivalents...) (Big thanks to Vincent Chu)
- Fixed a bug in vacc.c where atoms with radii less than 1A were not considered instead of atoms with no radii.
- Fixed error in tools/mesh/dx2mol.c (Thanks to Fred Damberger)
- Fixed floating point error which resulted in improper grid spacings for some cases.
- Fixed a bug in Vacc_molAcc which generates spurious regions of high internal dielectric for molecular surface-based dielectric definitions. These regions were very small and apparently affected energies by 1-2% (when used with the 'srfm mol'; the 'srfm smol' can potentially give larger deviations). The new version of the molecular surface is actually faster (requires 50-70% of the time for most cases) but we should all be using the spline surface anyway – right? (Thanks to John Mongan and Jessica Swanson for finding this bug).
- Fixed a bug in vpmg.c that caused an assertion error when writing out laplacian maps (Thanks to Vincent Chu).
- Ensured Vpmg::ccf was always re-initialized (in the case where the Vpmg object is being re-used).
- Removed a spurious error estimation in finite element calculations.
- Clarified the role of ccf and other variables in mypde.f and vpmg.c by expanding/revising the inline comments.

PDB2PQR 1.0.2 (2005-12)

New features

- Added ability for users to add their own forcefield files. This should be particularly useful for HETATMs.
- Added sdens keyword to inputgen.py to make PDB2PQR compatibile with APBS 0.4.0.
- Added a new examples directory with a basic runthrough on how to use the various features in PDB2PQR.

Bug fixes

- Fixed a bug that was unable to handle N-Terminal PRO residues with hydrogens already present.
- Fixed two instances in the PropKa routines where warnings were improperly handled due to a misspelling.
- Fixed instance where chain IDs were unable to be assigned to proteins with more than 26 chains.

PDB2PQR 1.1.0 (2006-04)

New features

- Structural data files have been moved to XML format. This should make it easier for users and developers to contribute to the project.
- Added an extensions directory for small scripts. Scripts in this directory will be automatically loaded into PDB2PQR has command line options for post-processing, and can be easily customized.
- Code has been greatly cleaned so as to minimize values hard-coded into functions and to allow greater customizability via external XML files. This includes a more object-oriented hierarchy of structures.
- Improved detection of the termini of chains.
- Assign-only now does just that - only assigns parameters to atoms without additions, debumping, or optimizations.
- Added a –clean command line option which does no additions, optimizations, or forcefield assignment, but simply aligns the PDB columns on output. Useful for using post-processing scripts like those in the extensions directory without modifying the original input file.
- The –userff flag has been replaced by opening up the –ff option to user-defined files.
- Pydoc documentation is now included in html/pydoc.
- A programmer's guide has been included to explain programming decisions and ease future development.
- A –ffout flag has been added to allow users to output a PQR file in the naming scheme of the desired forcefield.
- User guide FAQ updated.
- The efficiency of the hydrogen bonding detection script (–hbond) has been greatly improved.
- Increased the number of options available to users via the PDB2PQR web server.

Bug fixes

- Updated psize.py to use centers and radii when calculating grid sizes (thanks to John Mongan)
- Fixed bug where PDB2PQR could not read PropKa results from chains with more than 1000 residues (thanks to Michael Widmann)

PDB2PQR 1.1.1 (2006-05)

Bug fixes

- Fixed a bug which prevented PDB2PQR from recognizing atoms from nucleic acids with "*" in their atom names. (thanks to Jaichen Wang)
- Fixed a bug in the hydrogen bonding routines where a misnamed object led to a crash for very specific cases. (thanks to Josh Swamidass)

PDB2PQR 1.1.2 (2006-06)

Bug fixes

- Fixed a bug in the hydrogen bonding routines where PDB2PQR attempted to delete an atom that had already been deleted. (thanks to Rachel Burdge)
- Fixed a bug in chain detection routines where PDB2PQR was unable to detect multiple chains inside a single unnamed chain (thanks to Rachel Burdge)
- Fixed a second bug in chain detection routines where HETATM residues with names ending in "3" were improperly chosen for termini (thanks to Reut Abramovich)
- Fixed a bug where chains were improperly detected when only containing one HETATM residue (thanks to Reut Abramovich)

APBS 0.5.0 (2007-01)

New features

- Significantly streamlined the configure/build/install procedure:
  - Most common compiler/library options now detected by default
  - MALOC is now included as a "plugin" to simplify installation and compatibility issue
- Added new APOLAR section to input file and updated documentation – this function renders tools/manip/acc obsolete.
- Added support for standard one-character chain IDs in PQR files.
- Added a new "spl4" charge method (chgm) option to support a quintic B-spline discretization (thanks to Michael Schnieders).
- Updated psize.py
- Added a new "spl4" ion-accessibility coefficient model (srfm) option that uses a 7th order polynomial. This option provides the higher order continuity necessary for stable force calculations with atomic multipole force fields (thanks to Michael Schnieders).
- Modified the "sdh" boundary condition (bcfl) option to include dipoles and quadrupoles. Well-converged APBS calculations won't change with the dipole and quadrupole molecular moments included in the boundary potential estimate, but calculations run with the boundary close to the solute should give an improved result (thanks to Michael Schnieders).
- Updated documentation to reflect new iAPBS features (NAMD support)
- Added Gemstone example to the tutorial

- New example demonstrating salt dependence of protein-RNA interactions.
- Added code to allow for an interface with TINKER (thanks to Michael Schnieders).
- The Python wrappers are now disabled by default. They can be compiled by passing the –enable-python flag to the configure script. This will allow users to attempt to compile the wrappers on various systems as desired.
- Added XML support for reading in parameter files when using PDB files as input. New XML files can be found in tools/conversion/param/vparam.
- Added XML support for reading "PQR" files in XML format.
- Added support for command line –version and –help flags.
- Added support for XML output options via the –output-file and –output-format flags.
- Updated runme script in ion-pmf example to use environmental variable for APBS path
- Modified the license to allow exceptions for packaging APBS binaries with several visualization programs. PMG license modifed as well.
- Added a DONEUMANN macro to vfetk.c to test FEM problems with all Neumann boundary conditions (e.g., membranes).
- Added Vpmg_splineSelect to select the correct Normalization method with either cubic or quintic (7th order polynomial) spline methods.
- Modified the selection criteria in Vpmg_qfForce, Vpmg_ibForce and Vpmg_dbnpForce for use with the new spline based (spl4) method.
- Added ion-pmf to the make test suite.
- Updated splash screen to include new PMG acknowledgment
- Added runGB.py and readGB.py to the Python utilities, which calculate solvation energy based on APBS parameterized Generalized Born model.
- Updated authorship and tool documentation
- Deprecated ELEC->gamma keyword in lieu of APOLAR->gamma

Bug fixes and API changes

- Cleanup of documentation, new Gemstone example
- Clarified usage of dime in mg-para ELEC statements
- Massive cleanup of NOsh, standardizing molecule and calculation IDs and making the serial focusing procedure more robust
- Removed MGparm partOlap* data members; the parallel focusing centering is now done entirely within NOsh
- Updated the user manual and tutorial
- Updated psize.py to use centers and radii when calculating grid sizes (thanks to John Mongan)
- Fixed problems with FEM-based NPBE, LPBE, and LRPBE calculations
- Fixed a minor bug in the configure script that prevented MPI libraries from being found when using certain compilers.
- Updated acinclude.m4, aclocal.m4, config/* for new version (1.9) of automake and compatibility with new MALOC
- Fixed a bug where reading in a file in PDB format had atom IDs starting at 1 rather than 0, leading to a segmentation fault.

- Fixed a bug in mypde.f where double precision values were initialized with single precision number (causing multiplication errors).
- Fixed a bug in the FEM code. Now calls the npbe solver works properly with FEtk 1.40
- Modified the FEMParm struct to contain a new variable pkey, which is required for selecting the correct path in AM_Refine

PDB2PQR 1.2.0 (2007-01)

New features

- Added autoconf support for pdb2pka directory.
- Added new support for passing in a single ligand residue in MOL2 format via the –ligand command. Also available from the web server (with link to PRODRG for unsupported ligands).
- Numerous additions to examples directory (see examples/index.html) and update to User Guide.

Bug fixes

- Fixed charge assignment error when dealing with LYN in AMBER.
- Fixed crash when a chain has a single amino acid residue. The code now reports the offending chain and residue before exiting.
- Fixed hydrogen optimization bug where waters with no nearby atoms at certain orientations caused missing hydrogens.

PDB2PQR 1.2.1 (2007-04)

New features

- Updated documentation to include instructions for pdb2pka support, references, more pydoc documents.
- Added ligand examples to examples/ directory
- Added native support for the TYL06 forcefield. For more information on this forcefield please see Tan C, Yang L, Luo R. How well does Poisson-Boltzmann implicit solvent agree with explicit solvent? A quantitative analysis. Journal of Physical Chemistry B. 110 (37), 18680-7, 2006.
- Added a new HTML output page which relays the different atom types between the AMBER and CHARMM forcefields for a generated PQR file (thanks to the anonymous reviewers of the latest PDB2PQR paper).

Bug fixes

- Fixed bug where a segmentation fault would occur in PropKa if the N atom was not the first atom listed in the residue
- Fixed error message that occurred when a blank line was found in a parameter file.
- Better error handling in MOL2 file parsing.
- Fixed bug where ligands were not supported on PDB files with multiple MODEL fields.

APBS 0.5.1 (2007-07)

New features

- Replaced APOLAR->glen and APOLAR->dime keywords with APOLAR->grid
- Deprecated mergedx. Added mergedx2
  - mergedx2 takes the bounding box that a user wishes to calculate a map for, as well as a resolution of the output map. An output map meeting those specifications is calculated and store.
- Added pKa tutorial
- Added warning about strange grid settings (MGparm)
- Fixed a bug in vpmg.c that occured when a user supplied a dielectric map with the ionic strength set to zero, causing the map to not be used.
- Removed deprecated (as of 0.5.0) tools/manip/acc in lieu of new APOLAR APBS features
- Added enumerations for return codes, new PBE solver (SMPBE) and linear/ nonlinear types
- Added in code for Size-Modified PBE (SMPBE)

Bug fixes and API changes

- Fixed buffer over-run problem
- Fixed case inconsistency with inputgen.py and psize.py scripts which caused problems with some versions of Python
- Fixed bug wherein 'bcfl sdh' behaved essentially like 'bcfl zero'. Now we have the correct behavior: 'bcfl sdh' behaves like 'bcfl mdh' thanks to the multipole code added by Mike Schnieders. Interestingly, this bug didn't have a major on the large-molecule test cases/examples provided by APBS but did affect the small molecule solvation energies. Thanks to Bradley Scott Perrin for reporting this bug.
- Added support for chain IDs in noinput.py
- Fixed bug in noinput.py where REMARK lines would cause the script to fail.

PDB2PQR 1.3.0 (2008-01)

New features

- Added "make test" and "make adv-test"
- Fixed problems with "make dist"
- Added integration with Opal for launching jobs as well as querying status
- The user may use NUMPY to specify the location of NUMPY.
- Both PDB2PKA and PROPKA are enabled by default. PDB2PKA is enabled by default since ligand parameterization would fail without this option.
- For a regular user, "make install" tells the user the exact command the system administrator will use to make the URL viewable.
- The default value of 7.00 for the pH on the server form is removed due to a problem with browser refershing.
- Updated warning messages for lines beginning with SITE, TURN, SSBOND and LINK.

- Switched license from GPL to BSD.
- Made a new tar ball pdb2pqr-1.3.0-1.tar.gz for Windows users who cannot create pdb2pqr.py through configure process.
- configure now automatically detects SRCPATH, WEBSITE, and the location of pdb2pqr.cgi. In version 1.2.1, LOCALPATH(SRCPATH) and WEBSITE were defined in src/server.py and the location of pdb2pqr.cgi was specified in html/server.html (index.html). Configure now uses variable substitution with new files src/server.py.in and html/server.html.in to create src/server.py and html/server.html (index.html).
- SRCPATH is automatically set to the current working directory. WEBSITE is automatically set to http://fully_qualified_domain_name/pdb2pqr. Path to CGI is automcailly set to http://fully_qualified_domain_name/pdb2pqr/pdb2pqr.cgi.
- In version 1.2.1, there were 3 variables that needed to be changed to set up a server at a location different from agave.wustl.edu. LOCALPATH, WEBSITE, and the location of the CGI file. In this version, LOCALPATH has been used to SRCPATH to avoid confusion, since LOCALPATH could be interpreted as the local path for source files or the localpath for the server.
- Since configure now automatically sets the locations of files/directories based on the machine and configure options, the default agave.wustl.edu locations are not used anymore.
- A copy of pdb2pqr.css is included.
- configure prints out information about parameters such as python flags, srcpath, localpath, website, etc.
- configure now automatically creates tmp/ with r + w + x permissions.
- configure now automatically copies pdb2pqr.py to pdb2pqr.cgi.
- configure now automatically copies html/server.html to index.html after variable substitution. In src/server.py.in (src/server.py), WEBNAME is changed to index.html.
- ${HOME}/pdb2pqr is the default prefix for a regular user
- /var/www/html is the default prefix for root
- http://FQDN/pdb2pqr as default website.
- “make install” runs “make” first, and the copies the approprite files to –prefix.
- If root did not specify –prefix and /var/www/html/pdb2pqr already
- exists, then a warning is issued, and the user may choose to quit or overwrite that directory.
- Similary, if a regular user did not specify –prefix and ${HOME}/pdb2pqr already exists, then a warning is issued, and the user may choose to quit or overwrite that directory.
- If root does not specify –prefix to be a directory to be inside /var/www/html (for example, –prefix=/share/apps/pdb2pqr), then a symbolic link will be made to /var/www/html/pdb2pqr during “make install”.
- configure option –with-url can be specified either as something like http://sandstone.ucsd.edu/pdb2pqr-test or sandstone.ucsd.edu/pdb2pqr-test. It also doesn’t matter if there’s a ‘/’ at the end.
- If user is root, and the last part of URL and prefix are different, for example, –with-url=athena.nbcr.net/test0 –prefix=/var/www/html/pdb2pqr-test, then a warning will be issued saying the server will be viewable from the URL specified, but not the URL based on pdb2pqr-test. In other words, the server will be viewable from athena.abcr.net/test0, but not athena.nbcr.net/pdb2pqr-test. During “make install”, a symbolic link is created to enable users to view the server from –with-url.
- When making a symbolic link for root, if then link destination already exists as a directory or a symoblic link, then the user may choose to continue with creating the link and overwrite the original directory or quit.
- If the user changes py_path when running configure for PDB2PQR, then the change also applies to PROPKA.

Bug fixes

- Fixed the line feed bug. Now PDB2PQR handles different input files (.pdb and .mol2) created or saved on different platforms.
- Fixed "hbondwhatif" warning at start up.

Known issues

- The install directory name cannot contain dots.
- For python 2.2, if PDB2PQR cannot find module sets, then sets needs to be copied from .../python2.2/site-packages/MYSQLdb/sets.py to .../lib/python2.2

APBS 1.0.0 (2008-04)

New features

- Changed license to New BSD style open source license (see http://www.opensource.org/licenses/bsd-license.php) for more information
- Added in a feature limited version of PMG (Aqua) that reduces the memory footprint of an APBS run by 2-fold
- Modified several routines to boost the speed of APBS calculations by approximately 10% when combined with the low memory version of APBS
- Simplified parameter input for ION and SMPBE keywords (key-value pairs)
- Examples and documentation for size-modified PBE code (Vincent Chu et al)
- Added in "fast" compile-time option that uses optimized parameters for multigrid calculations
- mg-dummy calculations can be run with any number (n>3) of grid points
- Updated PMG license to LGPL
- Added per-atom SASA information output from APOLAR calculations
- Added per-atom verbosity to APOLAR calculation outputs
- Ability to read-in MCSF-format finite element meshes (e.g., as produced by Holst group GAMER software)
- Updated installation instructions in user guide
- Updated inputgen.py to write out the electrostatic potential for APBS input file.

Bug fixes

- Updated tools/python/apbslib* for new NOsh functionality
- Clarified ELEC/DIME and ELEC/PDIME documentation
- Added more transparent warnings/error messages about path lengths which exceed the 80-character limit
- Fixed small typo in user guide in installation instructions
- Fixed memory leaks throughout the APBS code
- Fixed NOsh_parseREAD errors for input files with r line feeds.
- Fixed a variable setting error in the test examples

- Fixed a bug where memory usage is reported incorrectly for large allocations on 64-bit systems
- Added DTRSV to APBS-supplied BLAS to satisfy FEtk SuperLU dependency
- Fixed a small bug in routines.c to print out uncharged molecule id
- Limited calculation of forces when surface maps are read in

APBS 1.1.0 (2009-03)

New features

- Moved APBS user guide and tutorial to MediaWiki
- Added in support for OpenMPI for parallel calculations
- Added in command line support for Opal job submissions (Code by Samir Unni)
- Allowed pathname containing spaces in input file, as long as the whole pathname is in quotes (“”)
- Documented ‘make test’ and related features

Modifications

- Modified the function bcCalc to march through the data array linearly when setting boundary conditions. This removes duplication of grid points on the edge of the array and corners.
- Clarified documentation on the IDs assigned to input maps, PQRs, parameter files, etc.
- pdated tutorial to warn against spaces in APBS working directory path in VMD; updated user guide to warn against spaces in APBS installation path on Windows
- ‘make test’ has been reconfigured to run before issuing make install (can be run from top directory)
- Removed tools/visualization/vmd from tools directory in lieu of built-in support in VMD
- Path lengths can now be larger than 80 characters
- Expanded authorship list
- Added in ‘make test-opal’ as a post install test (run from the examples install directory)
- Added additional concentrations to protein-rna test case to better encompass experimental conditions used by Garcia-Garcia and Draper; this improves agreement with the published data

Bug fixes

- Fixed typos in User Guide (ion keyword) and clarified SMPBE keyword usage
- Fixed typo in User Guide (writemat: poission -> poisson)
- Updated psize.py with Robert’s patch to fix inconsistent assignment of fine grid numbers in some (very) rare cases
- Fixed bug with boundary condition assignment. This could potentially affect all calculations; however, probably has limited impact: many test cases gave identical results after the bug fix; the largest change in value was < 0.07%.

PDB2PQR 1.4.0 (2009-03)

New features

- Updated html/master-index.html, deleted html/index.php.
- Updated pydoc by running genpydoc.sh.
- Added a whitespace option by by putting whitespaces between atom name and residue name, between x and y, and between y and z.
- Added radius for Chlorine in ligff.py.
- Added PEOEPB forcefield, data provided by Paul Czodrowski.
- Updated inputgen.py to write out the electrostatic potential for APBS input file.
- Updated CHARMM.DAT with two sets of phosphoserine parameters.
- Allowed amino acid chains with only one residue, using –assign-only option.
- Updated server.py.in so that the ligand option is also recorded in usage.txt.
- Updated HE21, HE22 coordinates in GLN according to the results from AMBER Leap program.
- Updated Makefile.am with Manuel Prinz's patch (removed distclean2 and appended its contents to distclean-local).
- Updated configure.ac, pdb2pqr-opal.py; added AppService_client.py and AppService_types.py with Samir Unni's changes, which fixed earlier problems in invoking Opal services.
- Applied two patches from Manuel Prinz to pdb2pka/pMC_mult.h and pdb2pka/ligand_topology.py.
- Updated PARSE.DAT with the source of parameters.
- Created a contrib folder with numpy-1.1.0 package. PDB2PQR will install numpy by default unless any of the following conditions is met:
- Working version of NumPy dectected by autoconf.
- User requests no installation with –disable-pdb2pka option.
- User specifies external NumPy installation.
- Merged Samir Unni's branch. Now PDB2PQR Opal and APBS Opal services are available (through –with-opal and/or –with-apbs, –with-apbs-opal options at configure stage).
- Added error handling for residue name longer than 4 characters.
- Updated hbond.py with Mike Bradley's definitions for ANGLE_CUTOFF and DIST_CUTOFF by default.
- Removed PyXML-0.8.4, which is not required for ZSI installation.
- Updated propka error message for make adv-test – propka requires a version of Fortran compiler.
- Updated na.py and PATCHES.xml so that PDB2PQR handles three lettered RNA residue names (ADE, CYT, GUA, THY, and URA) as well.
- Updated NA.xml with HO2' added as an alternative name for H2'', and H5" added as an alternative name for H5''.
- Updated version numbers in html/ and doc/pydoc/ .
- Updated web server. When selecting user-defined forcefield file from the web server, users should also provide .names file.
- Removed http://enzyme.ucd.ie/Services/pdb2pqr/ from web server list.

- Eliminated the need for protein when processing other types (ligands, nucleic acids).
- Updated psize.py with Robert Konecny's patch to fix inconsistent assignment of fine grid numbers in some (very) rare cases.
- Made whitespace option available for both command line and web server versions.
- Updated inputgen_pKa.py with the latest version.

Bug fixes

- Fixed a legacy bug with the web server (web server doesn't like ligand files generated on Windows or old Mac OS platforms).
- Fixed a bug in configure.ac, so that PDB2PQR no longer checks for Numpy.pth at configure stage.
- Updated pdb2pka/substruct/Makefile.am.
- Fixed isBackbone bug in definitions.py.
- Fixed a bug for Carboxylic residues in hydrogens.py.
- Fixed a bug in routines.py, which caused hydrogens added in LEU and ILE in eclipsed conformation rather than staggered.
- Fixed a bug in configure.ac, now it is OK to configure with double slashes in the prefix path, e.g., –prefix=/foo/bar//another/path
- Fixed a bug in nucleic acid naming scheme.
- Fixed a bug involving MET, GLY as NTERM, CTERM with –ffout option.
- Fixed a bug for PRO as C-terminus with PARSE forcefield.
- Fixed a bug for ND1 in HIS as hacceptor.
- Fixed the –clean option bug.
- Fixed a bug in CHARMM naming scheme.
- Fixed a bug in test.cpp of the simple test (which is related to recent modifications of 1AFS in Protein Data Bank).

APBS 1.2.0 (2009-10)

New features

- Updated NBCR opal service urls from http://ws.nbcr.net/opal/... to http://ws.nbcr.net/opal2/...
- Increased the number of allowed write statements from 10 to 20
- Updated inputgen.py with –potdx and –istrng options added, original modification code provided by Miguel Ortiz-Lombardía
- Added more information on PQR file parsing failures
- Added in support for OpenMP calculations for multiprocessor machines.
- Changed default Opal service from http://ws.nbcr.net/opal2/services/APBS_1.1.0 to http://sccne.wustl.edu:8082/opal2/services/apbs-1.2

Modifications

- Applied Robert Konecny's patch to bin/routines.h (no need to include apbscfg.h in routines.h)

Bug fixes

- Added a remove_Valist function in Python wrapper files, to fix a memory leak problem in pdb2pka
- Fixed a bug in smooth.c: bandwidth iband, jband and kband (in grid units) should be positive integers
- Fixed a bug in psize.py: for a pqr file with no ATOM entries but only HETATM entries in it, inputgen.py should still create an APBS input file with reasonable grid lengths
- Fixed a bug in Vgrid_integrate: weight w should return to 1.0 after every i, j or k loop is finished
- Fixed a bug in routines.c, now runGB.py and main.py in tools/python/ should be working again instead of producing segfault
- Fixed a few bugs in ApbsClient.py.in related to custom-defined APBS Opal service urls, now it should be OK to use custom-defined APBS Opal service urls for PDB2PQR web server installations

PDB2PQR 1.5 (2009-10)

New features

- APBS calculations can be executed through the PDB2PQR web interface in the production version of the server
- APBS-calculated potentials can be visualized via the PDB2PQR web interface thanks to Jmol
- Disabled Typemap output by default, added –typemap flag to create typemap output if needed.
- Enabled "Create APBS Input File" by default on the web server, so that APBS calculation and visualization are more obvious to the users.
- Added warnings to stderr and the REMARK field in the output PQR file regarding multiple occupancy entries in PDB file.
- Added more informative messages in REMARK field, explaining why PDB2PQR was unable to assign charges to certain atoms.
- Updated structures.py, now PDB2PQR keeps the insertion codes from PDB files.
- Added "make test-long", which runs PDB2PQR on a long list (246) of PDBs by default, it is also possible to let it run on specified number of PDBs, e.g., export TESTNUM=50; make test-long
- Updated NBCR opal service urls from http://ws.nbcr.net/opal/... to http://ws.nbcr.net/opal2/...
- Compressed APBS OpenDX output files in zip format, so that users can download zip files from the web server.
- Removed "EXPERIMENTAL" from APBS web solver interface and Jmol visualization interface.
- Updated all APBS related urls from http://apbs.sourceforge.net/... to http:/apbs.wustl.edu/...
- Merged PDB2PKA code, PDB2PKA is functional now.
- Added two new options: –neutraln and –neutralc, so that users can manually make the N-termini or C-termini of their proteins neutral.
- Added a local-test, which addresses the issue of Debian-like Linux distros not allowing fetching PDBs from the web.

- Added deprotonated Arginine form for post-PROPKA routines. This only works for PARSE forcefield as other forcefields lack deprotonated ARG parameters.
- Updated inputgen.py with –potdx and –istrng options added, original modification code provided by Miguel Ortiz-Lombardía.
- Changed default Opal service from http://ws.nbcr.net/opal2/services/pdb2pqr_1.4.0 to http://sccne.wustl.edu:8082/opal2/services/pdb2pqr-1.5

Bug fixes

- Verbosity outputs should be stdouts, not stderrs in web server interface. Corrected this in src/routines.py.
- Fixed a bug in psize.py: for a pqr file with no ATOM entries but only HETATM entries in it, inputgen.py should still create an APBS input file with reasonable grid lengths.
- Added special handling for special mol2 formats (unwanted white spaces or blank lines in ATOM or BOND records).
- Added template file to doc directory, which fixed a broken link in programmer guide.

APBS 1.2.1 (2009-12)

Bug fixes

- Added in warning into focusFillBound if there is a large value detected in setting the boundary conditions during a focusing calculation
- Added in a check and abort in Vpmg_qmEnergy if chopped values are detected. This occurs under certain conditions for NPBE calculations where focusing cuts into a low-dielectric regions.
- Fixed a bug in Vpmg_MolIon that causes npbe based calculations to return very large energies. This occurs under certain conditions for NPBE calculations where focusing cuts into a low-dielectric regions.

PDB2PQR 1.6 (2010-04)

New features

- Added Swanson force field based on Swanson et al paper (http://dx.doi.org/10.1021/ct600216k).
- Modified printAtoms() method. Now "TER" is printed at the end of every chain.
- Added Google Analytics code to get the statistics on the production server.
- Modified APBS calculation page layout to hide parameters by default and display PDB ID
- Added "make test-webserver", which tests a long list of PDBs (246 PDBs) on the production PDB2PQR web server.
- Removed `nlev` from `inputgen.py` and `inputgen_pKa.py` as nlev keyword is now deprecated in APBS.
- Added PARSE parameters for RNA, data from: Tang C. L., Alexov E, Pyle A. M., Honig B. Calculation of pKas in RNA: On the Structural Origins and Functional Roles of Protonated Nucleotides. Journal of Molecular Biology 366 (5) 1475-1496, 2007.

Bug fixes

- Fixed a minor bug: when starting `pka.py` from pdb2pka directory using command like "python pka.py [options] inputfile", we need to make sure scriptpath does not end with "/".
- Fixed a bug which caused "coercing to Unicode: need string or buffer, instance found" when submitting PDB2PQR jobs with user-defined force fields on Opal based web server.
- Fixed a bug in `main_cgi.py`, now Opal-based PDB2PQR jobs should also be logged in `usage.txt` file.
- Updated `src/utilities.py` with a bug fix provided by Greg Cipriano, which prevents infinite loops in analyzing connected atoms in certain cases.
- Fixed a bug related to neutraln and/or neutralc selections on the web server.
- Fixed a special case with `--ffout` and 1AIK, where the N-terminus is acetylated.
- Fixed a bug in `psize.py` per Michael Lerner's suggestion. The old version of `psize.py` gives wrong cglen and fglen results in special cases (e.g., all y coordinates are negative values).
- Fixed a bug in `main_cgi.py`, eliminated input/output file name confusions whether a PDB ID or a pdb file is provided on the web server.
- Fixed a bug which causes run time error on the web server when user-defined force field and names files are provided.
- Fixed a bug in `apbs_cgi.py`: pdb file names submitted by users are not always 4 characters long.

APBS 1.3 (2010-10)

New features

- Added in new read and write binary (gz) commands. Can read gzipped DX files directly.
- Added new write format to output the atomic potentials to a flat file (see atompot)
- Added new functionality for using a previously calculated potential map for a new calculation.
- Added a new program for converting delphi potential maps to OpenDX format. tools/mesh/del2dx
- Updated Doxygen manual with call/caller graphs. Replaced HTML with PDF.
- Added tools/matlab/solver with simple Matlab LPBE solver for prototyping, teaching, etc.
- Deprecated APBS XML output format.
- Deprecated nlev keyword.
- Added etol keyword, which allows user-defined error tolerance in LPBE and NPBE calculations (default errtol value is 1.0e-6).
- Added more explanatory error messages for the case in which parm keyword is missing from APBS input file for apolar calculations.
- Added a polar and apolor forces calculation example to examples/born/ .
- Added warning messages for users who try to compile APBS with –enable-tinker flag and run APBS stand-alone execution.
- Switched default Opal service urls from sccne.wustl.edu to NBCR.
- Added a sanity check in routines.c: 'bcfl map' in the input file requires 'usemap pot' statement in the input file as well.

- Introduced Vpmgp_size() routine to replace F77MGSZ call in vpmg.c
- Updated test results for APBS-1.3 release.

Bug fixes

- Modified Vpmg_dbForce with some grid checking code provided by Matteo Rotter.
- Fixed a bug in psize.py per Michael Lerner's suggestion. The old version of psize.py gives wrong cglen and fglen results in special cases (e.g., all y coordinates are negative values).
- Fixed a bug in examples/scripts/checkforces.sh: the condition for "Passed with rounding error" is abs(difference) < errortol, not the other way around.
- Fixed the help string in ApbsClient.py .
- Fixed a bug in Vacc_atomdSASA(): the atom SASA needs to be reset to zero displacement after finite melement methods.
- Fixed a bug in Vpmg_dbForce(): the initialization of rtot should appear before it is used.
- Fixed a bug in initAPOL(): center should be initialized before used.
- Fixed a bug in routines.c: eliminated spurious "Invalid data type for writing!" and "Invalid format for writing!" from outputs with "write atompot" statement in the input file.
- Fixed a bug in vpmg.c: fixed zero potential value problem on eges and corners in non-focusing calculations.

PDB2PQR 1.7 (2010-10)

- For PDB2PQR web interface users: the JMol web interface for APBS calculation visualization has been substantially improved, thanks to help from Bob Hanson. Those performing APBS calculations via the PDB2PQR web interface now have a much wider range of options for visualizing the output online – as well as downloading for offline analysis.
- For PDB2PQR command-line and custom web interface users: the Opal service URLs have changed to new NBCR addresses. Old services hosted at .wustl.edu addresses have been decommissioned. Please upgrade ASAP to use the new web service. Thank you as always to the staff at NBCR for their continuing support of APBS/PDB2PQR web servers and services.

PDB2PQR 1.7.1 (2011-08)

New features

- Switched Opal service urls from sccne.wustl.edu to NBCR.
- Added more JMol controls for visualization, JMol code and applets provided by Bob Hanson.
- Changed default forcefield to PARSE in web interface.

Bug fixes

- Fixed crash when opal returns an error.
- Fixed specific combinations of command-line arguments causing `pdb2pqr.py` to crash.
- Fixed opal job failing when filenames have spaces or dashs.

- Fixed gap in backbone causing irrationally placed hydrogens.
- Fixed crash when too many fixes are needed when setting termini.
- Corrected web and command line error handling in many cases.
- Fixed `--username` command line option.
- Fixed ambiguous user created forcefield and name handling. Now `--username` is required if `--userff` is used.
- Fixed `querystatus.py` not redirecting to generated error page.

PDB2PQR 1.7.1a (2011-09-13)

New features

- Added force field example.

Bug fixes

- Fixed ligand command line option.
- Fixed capitalization of force field in PQR header.
- Fixed error handling for opal errors.
- Fixed web logging error when using ligand files, user force fields, and name files.
- Fixed extension template in documentation.
- Fixed 1a1p example README to reflect command line changes.

PDB2PQR 1.8 (2012-01)

New Features

- Updated PROPKA to version 3.0
- Added residue interaction energy extension
- Added protein summary extension
- Combined hbond and hbondwhatit into one extension (hbond) with new command line parameters
- Combined rama, phi, psi into one extension (rama) with new command line parameters.
- Extensions may now add their own command line arguments. Extensions with their own command line arguments will be grouped separately.
- Improved interface for extensions
- Added Opal configuration file.

Bug Fixes

- Cleaned up white space in several files and some pydev warnings
- Creating print output no longer clears the chain id data from atoms in the data. (Affected resinter plugin)
- Removed possibility of one plug-in affecting the output of another
- Fixed –protonation=new option for propka30
- Improved time reporting for apbs jobs
- Fixed opal runtime reporting
- Fixed misspelled command line options that prevented the use of PEOEPB and TYL06
- Fixed error handling when certain data files are missing
- Fixed LDFLAGS environment variable not being used along with python specific linker flags to link Algorithms.o and _pMC_mult.so
- Fixed possible Attribute error when applying naming scheme.

APBS 1.4.0 (2012-07)

Summary

We are pleased to announce the release of APBS 1.4.0. This version of APBS includes a massive rewrite to eliminate FORTRAN from the software code base to improve portability and facilitate planned optimization and parallelization activities. A more detailed list of changes is provided below. Starting with this release, we have created separate installation packages for the APBS binaries, examples, and programming documentation. This change is in response to user requests and recognition of the large size of the examples and documentation directories.

Detailed changes

- Removed FORTRAN dependency from APBS
- Direct line by line translation of all source from contrib/pmgZ
- Functions replaced and tested incrementally to ensure code congruence
- Created new subfolder src/pmgC for translated pmg library
- Created new macros for 2d, 3d matrix access
- In src/generic/apbs/vmatrix.h
- Simulate native FORTRAN 2 and 3 dimensional arrays
- Use 1-indexed, column-major ordering
- Allowed direct 1-1 translation from FORTRAN to ensurre code congruence
- Added additional debugging and output macros to src/generic/apbs/vhal.h
- Added message, error message, assertion, warning, and abort macros
- Macro behavior modified by the –enable-debug flag for configure
- Non-error messages directed to stderr in debug, io.mc otherwise
- All error messages are directed to stdout
- In debug mode, verbose location information is provided

- Added additional flags to configure
- –with-fetk replaces FETK_INCLUDE, FETK_LIBRARY environment flags
- –with-efence enables compiling with electric fence library
- –enable-debug eliminates compiling optimization and includes line no info
- —enable-profiling adds profiling information and sets –enable-debug
- –enable-verbose-debug prints lots of function specific information

PDB2PQR 1.9 (2014-03)

New features

- Binary builds do not require python or numpy be installed to use. Everything needed to run PDB2PQR is included. Just unpack and use.
- OSX binaries require OSX 10.6 or newer. The OSX binary is 64-bit.
- Linux binaries require CentOS 6 or newer and have been tested on Ubuntu 12.04 LTS and Linux Mint 13. If you are running 64-bit Linux use the 64-bit libraries. In some cases the needed 32-bit system libraries will not be installed on a 64-bit system.
- Windows binaries are 32 bit and were built and tested on Windows 7 64-bit but should work on Windows XP, Vista, and 8 both 32 and 64-bit systems.
- PDB2PQR can now be compiled and run on Windows using MinGW32. See http://mingw.org/ for details.
- PDB2PQR now uses Scons for compilations. With this comes improved automated testing.
- A ligand file with duplicate atoms will cause pdb2pqr to stop instead of issue a warning. Trust us, this is a feature, not a bug!
- Improved error reporting.
- Added support for reference command line option for PROPKA.
- Added newresinter plugin to provide alternate methods for calculating interaction energies between residues.
- Mol2 file handling is now case insensitive with atom names.
- PROPKA with a pH of 7 is now specified by default on the web service.
- Compilation is now done with scons.
- Verbose output now includes information on all patches applied during a run.
- Added stderr and stdout to web error page.
- Added warning to water optimization when other water is ignored.
- Command line used to generate a pqr is now duplicated in the comments of the output.
- Added support for NUMMDL in parser.
- Added complete commandline feature test. Use complete-test target.
- Added propka support for phosphorous sp3. - Thanks to Dr. Stefan Henrich
- Added a PyInstaller spec file. Standalone pdb2pqr builds are now possible.

Bug fixes

- Rolled back change that prevented plugins from interfering with each other. Large proteins would cause a stack overflow when trying to do a deep copy
- Updated INSTALL file to reflect no more need for Fortran.
- Fixed apbs input file to match what web interface produces.
- Fixed user specified mobile ion species not being passed to apbs input file.
- Removed ambiguous A, ADE, C, CYT, G, GUA, T, THY, U, URA as possible residue names.
- Removed eval from pdb parsing routines.
- Updated web links where appropriate.
- Fixed hbond extension output to include insertion code in residue name.
- Fixed debumping routines not including water in their checks. Fixes bad debump of ASN B 20 in 1gm9 when run with pH 7.0.
- Fixed debumping failing to use best angle for a specific dihedral angle when no tested angles are without conflict.
- Fixed debumping using asymmetrical cutoffs and too large cutoffs in many checks involving hydrogen.
- Fixed debumping accumulating rounding error while checking angles.
- Fixed inconsistencies in pdb parsing. - Thanks to Dr. Stefan Henrich
- Fixed problems with propka handling of aromatic carbon/nitrogen. - Thanks to Dr. Stefan Henrich
- Fixed case where certain apbs compile options would break web visualization.
- Fixed improper handling of paths with a '.' or filenames with more than one '.' in them.

Known bugs

- If more than one extension is run from the command line and one of the extensions modifies the protein data structure it could affect the output of the other extension. The only included extensions that exhibit this problem are resinter and newresinter.

Other comments

- Removed numpy from contrib. The user is expected to have numpy installed and available to python at configuration.
- Support for numeric dropped.

APBS 1.4.1 (2014-08)

Summary

We are pleased to announced the release of APBS 1.4.1. This was primarily a bug fix release; however, we have added a few features we'd like to hightlight below. We would like to also highlight our new website, still located at: http://www.poissonboltzmann.org. This site is also hosted at GitHub and we hope that the new organization will make it easier for people to find the content they need. While we are still in the process of migrating some remaining content, we have added links to the previous page when needed. Thank you for your continuing support of APBS. As always, please use our mailing list to send up questions or comments about our software.

Detailed changes

- Multigrid bug fix for volumes with large problem domain.
- We have added a preliminary implementation of geometric flow.
- Finite element method support has been re-enabled.
- Migration of the APBS source tree to GitHub (http://github.com/Electrostatics/apbs-pdb2pqr) for better collaboration, issue tracking, and source code management.
- Improved test suite.

PDB2PQR 2.0.0 (2014-12)

New features

- Improved look of web interface.
- Option to automatically drop water from pdb file before processing.
- Integration of PDB2PKA into PDB2PQR as an alternative to PROPKA.
- Support for compiling with VS2008 in Windows.
- Option to build with debug headers.
- PDB2PKA now detects and reports non Henderson-Hasselbalch behavior.
- PDB2PKA can be instructed whether or not to start from scratch with `--pdb2pka-resume`.
- Can now specify output directory for PDB2PKA.
- Improved error regarding backbone in some cases.
- Changed time format on query status page.
- Improved error catching on web interface.

Bug fixes

- Fixed executable name when creating binaries for Unix based operating systems.<
- Fixed potential crash when using `--clean` with extensions.
- Fixed MAXATOMS display on server home page.
- PDB2PKA now mostly respects the `--verbose` setting.
- Fixed how hydrogens are added by PDB2PKA for state changes in some cases.
- Fixed psize error check.
- Will now build properly without ligand support if numpy is not installed.
- Removed old automake build files from all test ported to scons.
- Fixed broken opal backend.

Known bugs

- If more than one extension is run from the command line and one of the extensions modifies the protein data structure it could affect the output of the other extension. The only included extensions that exhibit this problem are resinter and newresinter.
- Running ligands and PDB2PKA at the same time is not currently supported.
- PDB2PKA currently leaks memory slowly. Small jobs will use about twice the normally required RAM (i.e. ~14 titratable residues will use 140MB). Big jobs will use about 5 times the normally required RAM (60 titratable residues will use 480MB). We are working on this.

Other comments

- Command line interface to PROPKA changed to accommodate PDB2PKA. PROPKA is now used with `--ph-calc-method=propka --with-ph` now defaults to 7.0 and is only required if a different pH value is required.
- `--ph-calc-method` to select optional method to calculate pH values used to protonate titratable residues. Possible options are "propka" and "pdb2pka".
- Dropped support for compilation with mingw. Building on Windows now requires VS 2008 installed in the default location.
- Updated included Scons to 2.3.3
- PDB2PKA can now be run directly (not integrated in PDB2PQR) with pka.py. Arguments are PDBfile and Output directory.
- No longer providing 32-bit binary build. PDB2PKA support is too memory intensive to make this practical in many cases.

PDB2PQR 2.1.0 (2015-12)

New features

- Added alternate method to do visualization using 3dmol.
- Replaced the Monte Carlo method for generating titration curves with Graph Cut. See http://arxiv.org/abs/1507.07021. If you prefer the Monte Carlo Method, please use http://nbcr-222.ucsd.edu/pdb2pqr_2.0.0/

Bug fixes

- Added compile options to allow for arbitrary flags to be added. Helps work around some platforms where scons does not detect the needed settings correctly.
- Fixed broken links on APBS submission page.
- Added some missing files to query status page results.
- Fixed some pages to use the proper CSS file.
- Better error message for `--assign-only` and HIS residues.
- Fixed PROPKA crash for unrecognized residue.
- Debumping routines are now more consistent across platforms. This fixes pdb2pka not giving the same results on different platforms.

Known bugs

- If more than one extension is run from the command line and one of the extensions modifies the protein data structure it could affect the output of the other extension. The only included extensions that exhibit this problem are resinter and newresinter.
- Running ligands and PDB2PKA at the same time is not currently supported.
- PDB2PKA currently leaks memory slowly. Small jobs will use about twice the normally required RAM (i.e. ~14 titratable residues will use 140MB). Big jobs will use about 5 times the normally required RAM (60 titratable residues will use 480MB). We are working on this.

Other comments

- Added fabric script used to build and test releases.
- The newtworkx library is now required for pdb2pka.

APBS 1.4.2.0 (2016-01)

Binary builds

Binary releases may be found on GitHub and on SourceForge.

New features

- Poisson-Boltzmann Semi-Analytical Method (PB-SAM) packaged and build with APBS.
- New Geometric flow API and improvements: https://github.com/Electrostatics/apbs-pdb2pqr/issues/235
- Support for BinaryDX file format: https://github.com/Electrostatics/apbs-pdb2pqr/issues/216
- SOR solver added for mg-auot input file option.
- DXMath improvements https://github.com/Electrostatics/apbs-pdb2pqr/issues/168 and https://github.com/Electrostatics/apbs-pdb2pqr/issues/216
- Test suite improvements:
  - APBS build in Travis-CI
  - Geometric Flow test added.
  - Protein RNA test enabled https://github.com/Electrostatics/apbs-pdb2pqr/issues/149
  - Intermediate result testing https://github.com/Electrostatics/apbs-pdb2pqr/issues/64
- Example READMEs converted to markdown and updated with latest results.

Bug fixes

- OpenMPI (mg-para) functionality restored: https://github.com/Electrostatics/apbs-pdb2pqr/issues/190
- Fized parsing PQR files that contained records other than ATOM and HETATM: https://github.com/Electrostatics/apbs-pdb2pqr/issues/77 and https://github.com/Electrostatics/apbs-pdb2pqr/issues/214
- Geometrix Flow boundary indexing bug fixed.
- Build fixes:

  - Out of source CMake build are again working.
  - Python library may be built: https://github.com/Electrostatics/apbs-pdb2pqr/issues/372
  - CentOS 5 binary builds for glibc compability.
  - Pull requests merged.
- Removed irrelevant warning messages: https://github.com/Electrostatics/apbs-pdb2pqr/issues/378

Notes

- The following packages are treated as submodules in APBS:
  - Geometric Flow has been moved to its own repository: https://github.com/Electrostatics/geoflow_c/
  - FETk has been cloned: https://github.com/Electrostatics/FETK/
  - PB-SAM lives here: https://github.com/Electrostatics/PB-SAM/
- Added chat feature for users.

Known bugs

- Travis-CI Linux builds are breaking because Geometric Flow relies on C++11 and Travis boxen have an old GCC that does not support C++11. This is also an issue for CentOS 5.
- BEM is temporarily disabled due to build issues.
- Geometric Flow build is currently broken on Windows using Visual Studio.

APBS 1.4.2.1 (2016-01)

New features

- Poisson-Boltzmann Semi-Anlytical Method (PB-SAM) packaged and built with APBS.
- New Geometric flow API and improvements in speed.
- Support for BinaryDX file format.
- SOR solver added for mg-auto input file option.
- DXMath improvements.
- Test suit improvements: * APBS build in Travis-CI * Geometric Flow tests added. * Protein RNA tests enabled. * Intermediate results testing.
- Example READMEs onverted to markdown and updated with latest results.

Bug fixes

- OpenMPI (mg-para) functionality restored.
- Fixed parsing PQR files that contained records other than ATOM and HETATM.
- Geometric Flow boundary indexing bug fixed.
- Build fixes: * Out of source CMake build are again working. * Python library may be built. * CentOS 5 binary builds for glibc compatibility. * Pull requests merged.

- Removed irrelevant warning messages.

Notes

The following packages are treated as submodules in APBS: * Geometric Flow has been moved to its own repository. * FETk has been cloned so that we could effect updates. * PB-SAM lives here: https://github.com/Electrostatics/PB-SAM

Added a chat feature for users.

Known bugs

- Travis CI Linux builds are breaking because Geometric Flow relies on C++11 and Travis boxen have an old GCC that does not support C++11. This also and issue for CentOS 5.
- BEM is temporarily disabled due to build issues.
- Geometric Flow build is currently broken on Windows using Visual Studio.

PDB2PQR 2.1.1 (2016-03)

New features

- Replaced the Monte Carlo method for generating titration curves with Graph Cut. See http://arxiv.org/1507.07021/

Bug fixes

- Added a check before calculating pKa's for large interaction energies

Known bugs

- If more than one extension is run from the command line and one of the extensions modifies the protein data structure it could affect the output of the other extension. The only included extensions that exhibit this problem are resinter and newresinter.
- Running ligands and PDB2PKA at the same time is not currently supported.
- PDB2PKA currently leaks memory slowly. Small jobs will use about twice the normally required RAM (i.e. ~14 titratable residues will use 140MB). Big jobs will use about 5 times the normally required RAM (60 titratable residues will use 480MB). We are working on this.

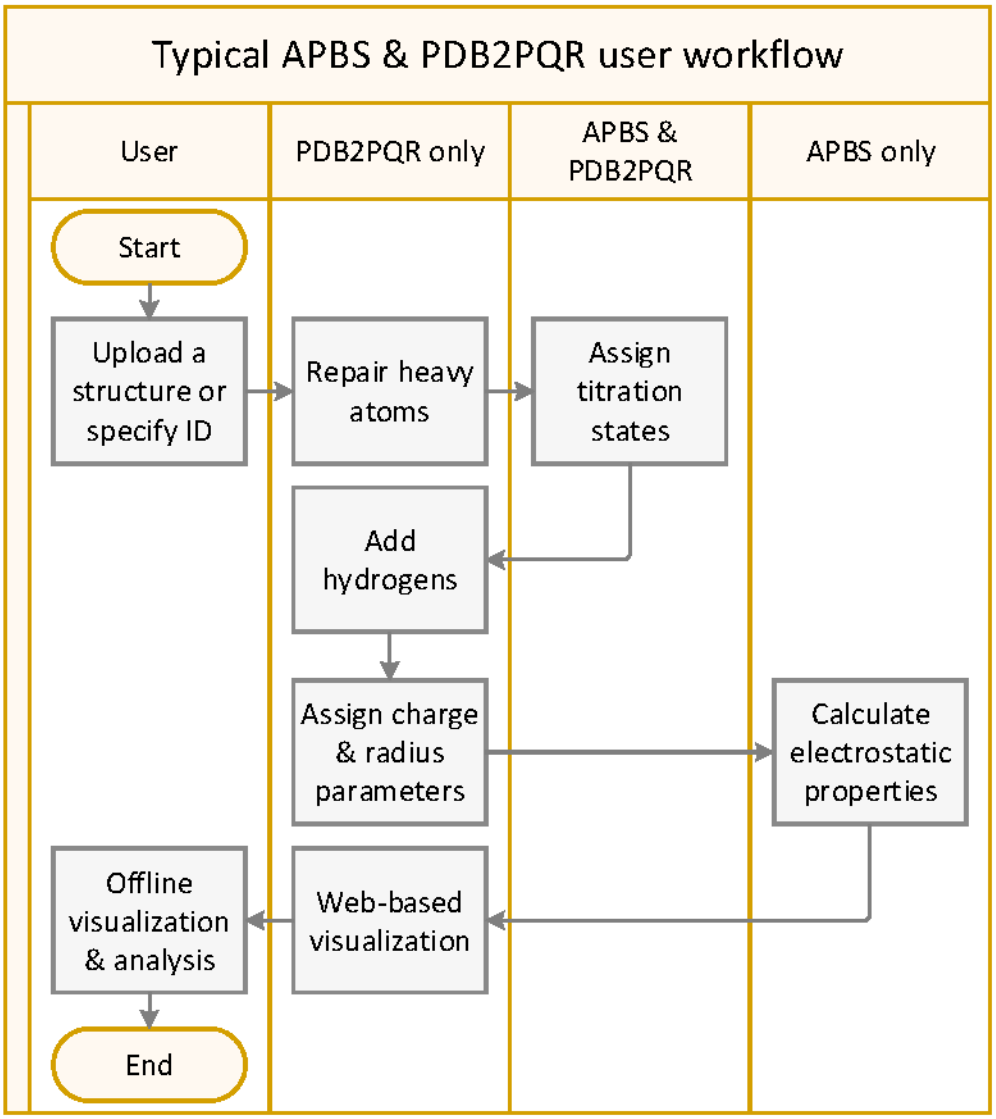
CHAPTER 3

Getting started

This section gives a basic overview of APBS-PDB2PQR workflows. It assumes that you have registered and obtained access to the software as described in *How to get the software*.

The basic APBS-PDB2PQR workflow involves a few simple steps, illustrated in the figure below and enumerated as:

1. Identify your molecular structure for *PDB2PQR* by specifying a PDB ID or uploading your own structure.
2. Use *PDB2PQR* to specify the titration state of the system, repair missing atoms, and assign parameters (charges and radii) to the atoms of your system.
3. Run *APBS* from within *PDB2PQR* or via the command line.
4. Visualize the results from within *PDB2PQR* or via *Other software*.


Typical APBS & PDB2PQR user workflow
User
PDB2PQR only
APBS & PDB2PQR
APBS only
Start
Upload a structure or specify ID
Repair heavy atoms
Assign titration states
Add hydrogens
Assign charge & radius parameters
Calculate electrostatic properties
Offline visualization & analysis
Web-based visualization
End

CHAPTER 4

Getting help

GitHub issues

Our preferred mechanism for user questions and feedback is via GitHub issues. We monitor these issues daily and usually respond within a few days.

Announcements

Announcements about updates to the APBS-PDB2PQR software and related news are available through our mailing list; please register for updates.

Old mailing lists

We continue to monitor the pdb2pqr-users and apbs-users mailing lists. However, we are in the process of phasing out these mailing lists (due to high spam content) in favor of user support through GitHub issues.

Contacting the authors

If all else fails, feel free to contact nathanandrewbaker@gmail.com.

CHAPTER 5

PDB2PQR

Installing PDB2PQR

Note: Please register before using PDB2PQR!

Most users will use PDB2PQR through the web server. However, it is also possible to install local versions of PDB2PQR. These local installations give a command line version of the PDB2PQR software that can be customized through a variety of extensions and used as a local web server (if compiled from source).

Binary installation

Everything needed to run PDB2PQR is included in the binary builds (including Python interpreter, dependencies, etc). Just unpack and use. PDB2PQR can be run with the "pdb2pqr" executable found in the base folder of the uncompressed archive.

Binary tarballs have `bin` in the file name and are named by target platform.

Binary builds *do not* provide local web server functionality. PDB2PQR must be compiled from source to provide a local web server.

Binaries are provided for the following platforms:

- OSX binaries require OSX 10.6 or newer. The OSX binary is 64-bit.
- Linux binaries require CentOS 6 or newer and have been tested on Ubuntu 12.04 LTS and Linux Mint 13. If you are running 64-bit Linux use the 64-bit libraries.
- Windows binaries are 64 bit and were built and tested on Windows 7 64-bit but should work on Windows XP, Vista, and 8 on 64-bit systems.

Source installation

As the bulk of the PDB2PQR code is written Python, the PDB2PQR code itself is (mostly) architecture- and compiler-independent. PDB2PQR has been tested using Python versions 2.6-2.7; PDB2PQR will not work with older versions of Python. Users who simply want to use the PDB2PQR without ligand parameterization support can unarchive the source code, change to the top-level source code directory, and run:

```
$ python scons/scons.py BUILD_PDB2PKA=False
$ python scons/scons.py install
```

If NumPy is unavailable, PDB2PQR will be built without ligand or PDB2PKA[1] support.

Configuring the installation

Compilation and installation can be configured by editing the `build_config.py` file. This is the preferred way to configure the program. Instructions and examples for each setting are included in the file.

Configuration command-line parameters can also be used and will override any settings in `build_config.py`:

`PREFIX=<DIR>` Set install directory. Default is `~/pdb2pqr`

`URL=<URL>` Set url for a local webserver. Default if `http://<COMPUTER NAME>/pdb2pqr/`

`APBS=<APBS_BINARY>` Location of APBS binary.

`OPAL=<OPAL_URL>` Set URL for the Opal web service.

`APBS_OPAL=<APBS_OPAL_URL>` Set URL for the APBS Opal web service.

`MAX_ATOMS=<MAX_ATOMS>` Sets the maximum number of atoms in a protein for non-Opal job submission. Only affects web tools. Default is 10000

`BUILD_PDB2PKA=False` Disable pkb2pka compilation.

Web server configuration

All the necessary files for web server installation are available with the PDB2PQR software; however, we would appreciate if users contact us before installing a publicly-accessible version of the web server so we can ensure that you are informed of PBD2PQR updates, etc.

Note: These instructions are intended for systems administrators with the ability to change the behavior of their web server software and/or install software in privileged locations.

To set up a server, edit the `build_config.py` file and set the `URL` and `PREFIX` to appropriate values then run the usual installation procedure:

```
$ python scons/scons.py
$ python scons/scons.py install
```

By default, the server is installed in `~/pdb2pqr` and the default URL is `http://computer_name/pdb2pqr`.

It is highly recommended that PREFIX and URL point to the same directory. Specifying `PREFIX=/var/www/html/pdb2pqr-test URL=http://somedomain/pdb2pqr-test` is recommened.

[1] PDB2PKA is the PDB2PQR library that includes both ligand parameterization and Poisson-Boltzmann-based pKa calculation routines. This code is written in C++ and Python. This portion of the code also requires the Python NumPy package.

If the server interface loads correctly but you cannot execute pdb2pqr by clicking the "Submit" button, make sure you have the permission to execute the `pdb2pqr.cgi` file. In particular, ensure that the access mode of `pdb2pqr.cgi` allows execution by the webserver (e.g., `chmod +x /var/www/html/pdb2pqr/pdb2pqr.cgi`). Additionally, you may need to change the configuration of your webserver to enable CGI execution.

Invoking PDB2PQR

Note: Please register before using PDB2PQR!

Most users will use PDB2PQR through the web server. However, it is also possible to install local versions of PDB2PQR and run these through the command line. This version of the software offers an expanded range of options and can also be customized with user extensions.

Todo

Make sure user extensions are adequately documented.

The command line PDB2PQR is invoked as

```
$ python pdb2pqr.py [options] --ff={forcefield} {path} {output-path}
```

This module takes a PDB file as input and performs optimizations before yielding a new PQR-style file in `{output-path}`. If `{path}` is a PDB ID it will automatically be retrieved from the online PDB archive.

Options

Todo

Replace this section with automagically generated documentation ala https://sphinx-argparse.readthedocs.io/en/stable/

Mandatory options

One of the options must be used for all PDB2PQR runs:

`--ff=FIELD_NAME` The forcefield to use - currently amber, charmm, parse, tyl06, peoepb and swanson are supported.

`--userff=USER_FIELD_FILE` A user-created forcefield file. Requires `--usernames` and overrides `--ff`.

`--clean` Do no optimization, atom addition, or parameter assignment, just return the original PDB file in aligned format. Overrides `--ff` and `--userff` options.

Titration state calculation options

`--ph-calc-method=PH_METHOD` Method used to calculate ph values. If a pH calculation method is selected, pKa values will be calculated and titratable residues potentially modified after comparison with the pH value supplied by `--with_ph` for each titratable residue

`PROPKA` Use PROPKA to calculate pKa values. PROPKA options include:

--propka-reference=PROPKA_REFERENCE Setting which reference values to use for stability calculations. See PROPKA 3.0 documentation for details.

--propka-verbose Print extra-verbose PROPKA information to `stdout`.

PDB2PKA Use PDB2PKA to calculate pKa values. Requires the use of the PARSE force field. Large proteins can take a very long time to run using this method. PDB2PKA options include:

--pdb2pka-out=PDB2PKA_OUT Output directory for PDB2PKA results. Defaults to `pdb2pka_output`.

--pdb2pka-resume Resume run from state saved in output directory.

--pdie=PDB2PKA_PDIE Protein dielectric constant. Defaults to 8.

--sdie=PDB2PKA_SDIE Solvent dielectric constant. Defaults to 80.

--pairene=PDB2PKA_PAIRENE Cutoff energy in (kT) for calculating interaction energies. Default: 1.0.

--with-ph=PH pH values to use when applying the results of the selected pKa calculation method to assign titration states. Defaults to 7.0.

Todo

Make sure that PDB2PQR force fields are referenced and described.

General options

--apbs-input Create a template APBS input file based on the generated PQR file. Also create a Python pickle for using these parameters in other programs.

--assign-only Only assign charges and radii - do not add atoms, debump, or optimize.

--chain Keep the PDB chain ID in the output PQR file.

--drop-water Drop waters before processing protein. Currently recognized and deleted are the following water types: `HOH`, `WAT`

--ffout=FIELD_NAME Instead of using the standard canonical naming scheme for residue and atom names, use the names from the given forcefield. Currently amber, charmm, parse, tyl06, peoepb and swanson are supported.

-h or --help Print help message and exit.

--ligand=PATH Calculate the parameters for the ligand in mol2 format at the given path. PDB2PKA must be compiled.

--neutraln Make the N-terminus of this protein neutral (default charge state is determined by pH and pKa). Requires PARSE force field.

--neutralc Make the C-terminus of this protein neutral (default is charged). Requires PARSE force field.

--nodebump Do not perform the debumping operation to remove steric clashes. See *debumping* for more information.

--noopts Do not perform hydrogen bond optimization. See *hbondopt* for more information.

--typemap Create a map of atom types in the molecule.

--usernames=USER_NAME_FILE The user created names file to use. Required if using `--userff`.

-v or --verbose Print additional information to stdout.

--version Show program's version number and exit

--whitespace Insert whitespaces between atom name and residue name, between x and y, and between y and z.

--include_header Include pdb header in pqr file.

> **Warning:** The resulting PQR file will not with APBS versions prior to 1.5.

Extension options

These options refer to extension modules distributed with PDB2PQR.

--chi Print the per-residue sidechain chi angles to *output-path*.chi

--contact Print a list of contacts to *output-path*.con

--hbond Print a list of hydrogen bonds to *output-path*.hbond. Additional options for this extension include:

- **--whatif** Change hbond output to WHAT-IF format.
- **--angle_cutoff=ANGLE_CUTOFF** Angle cutoff to use when creating hbond data (default 30.0 deg)
- **--distance_cutoff=DISTANCE_CUTOFF** Distance cutoff to use when creating hbond data (default 0.34 nm)
- **--old_distance_method** Use distance from donor hydrogen to acceptor to calculate distance used with --distance_cutoff.

--rama Print the per-residue phi and psi angles to *output-path*.rama for Ramachandran plots. Options for this extension include:

- **--phi_only** Only include phi angles in output. Rename output file *output-path*.phi
- **--psi_only** Only include psi angles in output. Rename output file *output-path*.psi

--resinter or --newresinter Print interaction energy between each residue pair in the protein to *output-path*.resinter or *output-path*.newresinter Additional options for this extension include:

- **--residue_combinations** Remap residues to different titration states and rerun --resinter, appending the output. Consider only the minimum number of whole protein titration combinations needed to test each possible pairing of residue titration states. Normally used with --noopt. If a protein titration state combination results in a pair of residue being re-tested in the same individual titration states, a warning will be generated if the re-tested result is different. This warning should not be possible if used with --noopt.
- **--all_residue_combinations** Remap residues to ALL possible titration state combinations and rerun resinter appending output. Results with --noopt should be the same as --residue_combinations. Runs considerably slower than --residue_combinations and generates the same type of warnings. Use without --noopt to discover how hydrogen optimization affects residue interaction energies via the warnings in the output.

--salt Print a list of salt bridges to *output-path*.salt

--summary Print protein summary information to *output-path*.summary

Method descriptions

Debumping

Unless otherwise instructed with `--nodebump`, PDB2PQR will attempt to remove steric clashes (debump) between residues.

To determine if a residue needs to be debumped, PDB2PQR compares its atoms to all nearby atoms. With the exception of donor/acceptor pairs and CYS residue SS bonded pairs, a residue needs to be debumped if any of its atoms are within cutoff distance of any other atoms. The cutoff is 1.0 angstrom for hydrogen/hydrogen collisions, 1.5 angstrom for hydrogen/heavy collisions, and 2.0 angstrom otherwise.

Considering the atoms that are conflicted, PDB2PQR changes selected dihedral angle configurations in increments of 5.0 degrees, looking for positions where the residue does not conflict with other atoms. If modifying a dihedral angle does not result in a debumped configuration then the dihedral angle is reset and the next one is tried. If 10 angles are tried without success the algorithm reports failure.

Warning: It should be noted that this is not an optimal solution. This method is not guaranteed to find a solution if it exists and will accept the first completely debumped state found, not the optimal state.

Additionally, PDB2PQR does not consider water atoms when looking for conflicts.

Hydrogen bond optimization

Unless otherwise indicated with `--noopts`, PDB2PQR will attempt to add hydrogens in a way that optimizes hydrogen bonding.

The hydrogen bonding network optimization seeks, as the name suggests, to optimize the hydrogen bonding network of the protein. Currently this entails manipulating the following residues:

- Flipping the side chains of HIS (including user defined HIS states), ASN, and GLN residues;
- Rotating the sidechain hydrogen on SER, THR, TYR, and CYS (if available);
- Determining the best placement for the sidechain hydrogen on neutral HIS, protonated GLU, and protonated ASP;
- Optimizing all water hydrogens.

Titration states

PDB2PQR has the ability to recognize certain protonation states and keep them fixed during optimization. To use this feature manually rename the residue name in the PDB file as follows:

Neutral ASP ASH

Negative CYS: CYM

Neutral GLU: GLH

Neutral HIS: HIE or HSE (epsilon-protonated); HID or HSD (delta-protonated)

Positive HIS: HIP or HSP

Neutral LYS LYN

Negative TYR TYM

PDB2PQR is unable to assign charges and radii when they are not available in the forcefield - thus this warning message will occur for most ligands unless a MOL2 file is provided for the ligand with the `--ligand` option. Occasionally this message will occur in error for a standard amino acid residue where an atom or residue may be

misnamed. However, some of the protonation states derived from the PROPKA results are not supported in the requested forcefield and thus PDB2PQR is unable to get charges and radii for that state. PDB2PQR currently supports the following states as derived from PROPKA:

Protonation State	AMBER Support	CHARMM Support	PARSE Support
Neutral N-Terminus	No	No	Yes
Neutral C-Terminus	No	No	Yes
Neutral ARG	No	No	No
Neutral ASP	Yes[1]	Yes	Yes
Negative CYS	Yes[1]	No	Yes
Neutral GLU	Yes[1]	Yes	Yes
Neutral HIS	Yes	Yes	Yes
Neutral LYS	Yes[1]	No	Yes
Negative TYR	No	No	Yes

Extending PDB2PQR

There are several ways to extend PDB2PQR to implement new functionality and new force fields.

Custom charge and radius parameters

Adding a few additional parameters to an existing forcefield

If you are just adding the parameters of a few residues and atoms to an existing forcefield (e.g., AMBER), you can open the forcefield data file distributed with PDB2PQR (`dat/AMBER.DAT`) directly and add your parameters. After the parameter addition, save the force field data file with your changes. You should also update the corresponding .names file (`dat/AMBER.names`) if your added residue or atom naming scheme is different from the PDB2PQR canonical naming scheme. See *PDB2PQR NAMES files* for more information about NAMES files.

Adding an entirely new forcefield

The following steps outline how to add a new force field to PDB2PQR.

You will need to generate a forcefield data file (e.g., `myff.DAT`) and, if your atom naming scheme of the forcefield is different from the PDB2PQR canonical naming scheme, you will also need to provide a names files (`myFF.names`). It is recommended to build your own forcefield data and names files based on existing PDB2PQR `.DAT` and `.names` examples provided with PDB2PQR in the `dat` directory. See *PDB2PQR NAMES files* for more information about NAMES files. After finishing your forcefield data file and names file, these can be used with either the command line or the web server versions of PDB2PQR.

Todo

Provide documentation of the PDB2PQR DAT and NAMES formats.

Adding new functionality

PDB2PQR provides an `extensions` directory that allows you to add your own code to the PDB2PQR workflow. All functions in the extensions directory are automatically loaded into PDB2PQR as command line options using the

[1] Only if residue is not a terminal residue; if the residue is terminal it will not be set to this state.

function's name, and are called after all other steps (optimization, atom addition, parameter assignment) have been completed. As a result any available functions are particularly useful for post-processing, or for analysis without any changes to the input structure by using the `--clean flag`.

One of the advantages of using PDB2PQR in this fashion is the ability to use built-in PDB2PQR functions. While a full and more detailed API can be found in the PDB2PQR `pydoc` documentation, some useful functions are listed below, organized by PDB2PQR module:

class `protein.`**Protein**
Protein objects

printAtoms(*atomlist*, *flag*)
Print a list of atoms

getResidues()
Return a list of residues

numResidues()
Return the number of residues

numAtoms()
Return the number of atoms

getAtoms()
Return a list of atom objects

getChains()
Return a list of chains

class `structures.`**Chain**
Biomolecule chain objects

getResidues()
Return a list of residues in the chain

numResidues()
Return the number of residues in the chain

numAtoms()
Return the number of atoms in the chain

getAtoms()
Return a list of atom objects in the chain

class `structures.`**Residue**
Biomolecule residue object (e.g., amino acid)

numAtoms()
Return the number of atoms in the residue

addAtom(*atom*)
Add the atom object to the residue

removeAtom(*name*)
Remove a specific atom from the residue

renameAtom(*old*, *new*)
Rename atom "old" with "new"

getAtom(*name*)
Return a specific atom from the residue

hasAtom(*name*)
Determine if the residue has the atom "name"

class structures.**Atom**
The atom of a residue

getCoords()
Return the x/y/z coordinates of the atom

isHydrogen()
Determine if the atom is a hydrogen or not

isBackbone()
Determine whether the atom is from the backbone

utilities.**getAngle**(*c1*, *c2*, *c3*)
Get the angle between the three coordinate sets

utilities.**getDihedral**(*c1*, *c2*, *c3*, *c4*)
Get the dihedral angle from the four coordinates

utilities.**distance**(*c1*, *c2*)
Return the distance between the two coordinates

utilities.**add**(*c1*, *c2*)
Return c1 + c2

utilities.**subtract**(*c1*, *c2*)
Return c1 - c2

utilities.**cross**(*c1*, *c2*)
Return the cross product of c1 and c2

utilities.**dot**(*c1*, *c2*)
Return the dot product of c1 and c2

utilities.**normalize**(*c1*)
Normalize the c1 coordinates (to unit length)

Todo

Incorporate PDB2PQR Python documentation into Sphinx rather than entering it here manually.

PDB2PQR license

Nathan A. Baker (nathanandrewbaker@gmail.com), Pacific Northwest National Laboratory

Additional contributing authors listed in the code documentation.

Redistribution and use in source and binary forms, with or without modification, are permitted provided that the following conditions are met:

- Redistributions of source code must retain the above copyright notice, this list of conditions and the following disclaimer.

- Redistributions in binary form must reproduce the above copyright notice, this list of conditions and the following disclaimer in the documentation and/or other materials provided with the distribution.
- Neither the names of University College Dublin, Battelle Memorial Institute, Pacific Northwest National Laboratory, US Department of Energy, or University of Marburg nor the names of its contributors may be used to endorse or promote products derived from this software without specific prior written permission.

CHAPTER 6

APBS

Installing APBS

Note: Please register before installing APBS.

The best way to install APBS is via the binary installation; see *How to get the software* for more information. We currently offer binaries for the Ubuntu platform on a variety of architectures as well as command-line binaries for WinXP and Mac OS X. For all other systems, please install from source on your particular platform and feel free to contact the APBS users mailing list for more help and/or to request a binary for that system.

Binary installation

Windows

If you are using APBS on a Windows system, you may not want to install APBS in a directory with spaces in the path name (e.g., `C:\Program Files\`) as this can cause problems with some visualization programs. The windows release is for Windows 7 and is 64-bit only. It installs to `C:\APBS` by default and provides a batch file that creates a shell with the correct path.

Mac OS X

The OS X build is built for Mavericks, available as a `.dmg` (disk image) file with an APBS Application Bundle. Just open the `.dmg` file and drag the app to the `Applications` folder. Running the App Bundle opens a Terminal window with the appropriate path to the APBS binary.

Linux

APBS binaries are provided in compressed tar format (`*.tgz`) for Linux. This tarball can be opened by

```
gzip -dc apbs-{#}.{#}.{#}-{XYZ}.tgz | tar xvf -
```

where `apbs-#.#.#-XYZ.tgz` is the downloaded tarball with `XYZ` as the particular architecture of the binary you downloaded and `#.#.#` as the version number. This will expand into a directory called `apbs-#.#.#-XYZ`. The contents of this directory can be placed anywhere on your system that you prefer (and have access to).

Source installation

We recommend that most users compile APBS from our official releases; see *How to get the software* for downloading instructions. Adventurous users may want to try to compile the developmental versions on GitHub. In either case, detailed compile/build instructions are provided with the source code.

What's in the box?

bin contains the main APBS executable

share/apbs contains additional APBS-related files

doc the APBS programmer guide

examples APBS examples

tests the APBS test suite

tools useful programs to help process APBS input and output

include header files for building software that calls APBS

lib libraries for building software that calls APBS

Invoking APBS

Unless invoked by *PDB2PQR* or another software package (see *Other software*), most APBS calculations are performed from the command line by running an APBS input file through the APBS program.

As mentioned in the installation and availability section, the main APBS binary is installed in `${APBS_PREFIX}/bin` where `${APBS_PREFIX}` is the top-level directory you chose for the installation. You can move the binary to any directory you choose.

APBS is invoked with a very simple syntax:

```
apbs [options] input-file
```

where the list of `[options]` can be obtained by running APBS with the `--help` option. The input file format is described in *APBS input files*.

The Opal Toolkit is software produced by NBCR. This toolkit allows for the computing load for processor intensive scientic applications to be shifted to a 3rd party and/or generic computing grid. This can be tremendously advantageous in situations where a large amount of computing power is not locally available, but is required, for the task at hand. In particular, many users have discovered that their local computational resources are insufficient for certain types of APBS calculations on large systems or at extremely high accuracy. This client removes this resource limitation by allowing users to run on clusters at NBCR. Recent developmental versions APBS add optional support for the off-loading of APBS calculations to an Opal service. Opal support has been integrated into APBS such that the end user will not be able to tell the difference between local and Opal runs of APBS: the APBS Opal client can be invoked in exactly the same way as the main APBS binary with identical output. The APBS Opal support is in the form of a

Python script `ApbsClient.py` and is installed by default. The script has been tested on Python 2.5; newer/older versions of Python may or may be functional. As mentioned above, the basic invocation is the same as the main binary.

```
ApbsClient.py [options] input-file
```

APBS input files

APBS input files are loosely-formatted files which contain information about the input, parameters, and output for each calculation.

These files are whitespace- or linefeed-delimited. Comments can be added to the input files via the # character; all text between the # and the end of the line is not parsed by APBS. If pathnames used in the input file contain spaces, then the entire pathname must be enclosed in quotes. For example, if you wanted to refer to the file `foo` which resides in a directory with spaces in its name, then you should refer to `foo` as `"/path with spaces/foo"`. Specific examples of APBS input are provided in *APBS-PDB2PQR examples and tutorials*.

APBS input files contain three basic sections which can be repeated any number of times:

READ input file section section for specifying input

ELEC input file section section for specifying polar solvation (electrostatics) calculation parameters

APOLAR input file section section for specifying apolar solvation calculation parameters

PRINT input file section section for specifying summary output

The APBS input file is constructed from these sections in the following format:

```
READ
...
END

ELEC
...
END

APOLAR
...
END

PRINT
...
END

QUIT
```

These sections can occur in any order and can be repeated any number of times. However, the sections are interdependent. For example, PRINT requires ELEC and/or APOLAR while ELEC requires one or more READ sections. Sections can also be repeated; several READ statements may be used to load molecules and multiple ELEC or APOLAR sections would specify various electrostatics calculations on one or more molecules.

Each section has the following syntax:

```
SECTION [name <id>]
```

where the optional `name` argument allows the user to include a string to identify the section. In the absence of this argument, sections are assigned numerical IDs.

READ input file section

The READ block of an APBS input file has the following general format:

```
READ
    [ keywords... ]
END
```

where `keywords` is or more of the keywords described below (the line breaks and indentation are for clarity; only whitespace is necessary).

Note: One of these sections must be present for every molecule involved in the APBS calculation. Molecule and "map" IDs are assigned implicitly assigned for each molecule/map read, based on order and starting at 1 and incremented independently for each input type. In other words, each input PQR file is assigned an ID 1, 2, 3, ...; each input dielectric map is assigned an independent ID 1, 2, 3, ...; etc.

charge

This command allows APBS to read the fixed (molecular) charge density function mapped to a mesh. The inputs are maps of charge densities; these values have units of e_c $Å^{-3}$, where e_c is the electron charge. In general, this command will read charge-maps written by *ELEC input file section write* commands. The syntax of this command is:

```
READ charge {format} {path} END
```

format Specify the format of the charge map. Acceptable values include:

- **dx** *OpenDX scalar data format*
- **gz** gzipped (zlib) compressed *OpenDX scalar data format*. Files can be read directly in compressed form.

path The location of the charge map file.

diel

This command allows APBS to read the dielectric function mapped to 3 meshes shifted by one-half grid spacing in the x, y, and z directions. The inputs are maps of dielectric variables between the solvent and biomolecular dielectric constants; these values are unitless. In general, this command will read dielectric maps written by by *ELEC input file section write* commands. The syntax of this command is:

```
READ diel {format} {path-x} {path-y} {path-z} END
```

format The format of the dielectric map.

- **dx** *OpenDX scalar data format*
- **gz** gzipped (zlib) compressed *OpenDX scalar data format*. Files can be read directly in compressed form.

path-x The location of the x-shifted dielectric map file.

path-y The location of the y-shifted dielectric map file.

`path-z` The location of the z-shifted dielectric map file.

Note: If you choose this option and have a non-zero ionic strength, you must also include a READ *kappa* statement.

kappa

This command allows APBS to read the ion-accessibility function mapped to a mesh. The inputs are maps of ion accessibility values which range between 0 and the build Debye-Hückel screening parameter; these values have units of $Å^{-2}$. In general, this command will read kappa-maps written by by *ELEC input file section write* commands. The syntax of this command is:

```
READ kappa {format} {path} END
```

format Specify the format of the charge map. Acceptable values include:

- **dx** *OpenDX scalar data format*
- **gz** gzipped (zlib) compressed *OpenDX scalar data format*. Files can be read directly in compressed form.

path The location of the map file.

Note: If you choose this option, you must also include a read diel statement.

---

mol

This command specifies the molecular data to be read into APBS. The syntax is

```
READ mol {format} {path} END
```

format The format of the input data.

- **pqr** Specify that molecular data is in *PQR format*.
- **pdb** Specify that molecular data is in pseudo-PDB format. If this type of structure file is used, then a parameter file must also be specified with a READ *parm* statement to provide charge and radius parameters for the biomolecule's atoms.

path The location of the molecular data file.

parm

This command specifies the charge and radius data to be used with pseudo-PDB-format molecule files. The syntax is:

```
READ parm {format} {path} END
```

format The format of the parameter file.

- **flat** Specify that the parameter file is in *APBS flat-file parameter format*.
- **xml** Specify that the parameter file is in *APBS XML parameter format*

path The location of the parameter data file.

Note: APBS provides a few example files as part of the source code distribution. Currently, example files only contain the polar parameters that can also be assigned more easily through the PDB2PQR software.

---

pot

This command allows APBS to read the electrostatic potential mapped to a mesh. The inputs are maps of the electrostatic potential from a previous calculation. In general, this command will read potential-maps written by by *ELEC input file section write* commands. The syntax of this command is:

```
READ pot {format} {path} END
```

format Specify the format of the charge map. Acceptable values include:

dx *OpenDX scalar data format*

gz gzipped (zlib) compressed *OpenDX scalar data format*. Files can be read directly in compressed form.

path The location of the map file.

Note: To use this functionality you must set the *bcfl* keyword to `map`. See also: *usemap*.

ELEC input file section

The ELEC block of an APBS input file is used for polar solvation (electrostatics) calculations and has the following syntax:

```
ELEC [ name {id} ]
     {type}
     {keywords...}
END
```

The optional `id` variable is a simple string that allows ELEC statements to be named. Since numerous ELEC blocks may appear in an APBS input file, it can be difficult to keep track of them all. It is possible to assign an optional name (string) to each ELEC block to simplify the organizational process.

The `type` command defines the types of ELEC calculation to be performed and includes:

- Finite difference multigrid calculations with PMG.
  - *mg-auto*
  - *mg-para*
  - *mg-manual*
- Geometric flow solvation finite difference calculations
  - *geoflow-auto*
- Boundary element method calculations with TABI-PB.
  - *tabi*
- Analytic and semi-analytic Poisson-Boltzmann approximations
  - *pbam-auto*
  - *pbsam-auto*
- Finite element calculations with FEtk.
  - *fe-manual*
- No-op modes for generating coefficient maps

- *mg-dummy*

Finally, the `keywords` are calculation-specific commands that customize the particular type of calculation. This section is the main component for polar solvation calculations in APBS runs. There may be several ELEC sections, operating on different molecules or using different parameters for multiple runs on the same molecule. The order of the ELEC statement can matter since certain types of boundary conditions (*bcfl*) can require information about previous calculations.

tabi

This mode uses the TABI-PB integral equation software from Geng and Krasny to solve the linearized Poisson-Boltmzann equation. Boundary element methods offer the ability to focus numerical effort on a much smaller region of the problem domain: the interface between the molecule and the solvent. In this method, two coupled integral equations defined on the solute-solvent boundary define a mathematical relationship between the electrostatic surface potential and its normal derivative with a set of integral kernels consisting of Coulomb and screened Coulomb potentials with their normal derivatives. The boundary element method requires a surface triangulation, generated by a program such as MSMS or NanoShaper, on which to discretize the integral equations.

For more information, see the Geng & Krasny 2013 J Comput Phys paper.

ion

Specify the bulk concentrations of mobile ion species present in the system. This command can be repeated as necessary to specify multiple types of ions; however, only the largest ionic radius is used to determine the ion-accessibility function. The total bulk system of ions must be electroneutral which means the charge densities/concentrations of positive and negative ions must be equal. The syntax is:

```
ion charge {charge} conc {conc} radius {radius}
```

where

`charge` Mobile ion species charge (floating point number in ec)

`conc` Mobile ion species concentration (floating point number in M)

`radius` Mobile ion species radius (floating point number in Å)

mac

TABI-PB parameter, multipole acceptance criterion (MAC), that controls distance ratio at which the method uses direct summation or Taylor approximation (a particle-cluster interaction) to calculate the integral kernels. The syntax is:

```
mac {theta}
```

where `theta` is a floating-point number from 0 to 1 controlling the distance ratio. This multipole acceptance criterion (MAC) is $\frac{r_c}{R} \leqslant \theta$, where r_c is the cluster radius, and R is the distance of the particle to the cluster center. If the above relationship is satisfied, the Taylor approximation will be used instead of direct summation. A typical value for this parameter is 0.8.

mesh

TABI-PB parameter that spceifies the meshing software used to generate surface mesh. The syntax is:

```
mesh {flag}
```

where `flag` is an integer indicating the meshing software to be used:

0 MSMS

1 SES implementation in NanoShaper

2 Skin surface implementation in NanoShaper

The default avlue is MSMS. Note that the executables for MSMS and NanoShaper must be included in your path to use them.

Todo

The integer flag values for `mesh` should be replaced by human-readable strings. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/496

mol

This term specifies the molecule for which the calculation is to be performed. The syntax is:

```
mol {id}
```

where `id` is the integer ID of the molecule for which the apolar calculation is to be performed. The molecule IDs are based on the order in which molecules are read by `READ mol` statements (see *READ input file section*), starting from 1.

outdata

TABI-PB parameter that specifies the file type for printing the output data. The syntax is:

```
outdata {flag}
```

where `flag` is an integer indicating the output file types:

0 .dat format

1 Both the .dat format and a VTK polygonal data file that can be visualized in the ParaView software. The VTK file contains color mappable potentials and normal derivatives of potentials on the faces and vertices of the mesh.

Todo

The integer flag values for `mesh` should really be replaced by human-readable strings.

pdie

Specify the dielectric constant of the solute molecule. The syntax is:

```
pdie {diel}
```

where `diel` is the floating point value of the unitless biomolecular dielectric constant. This is usually a value between 2 to 20, where lower values consider only electronic polarization and higher values consider additional polarization due to intramolecular motion. The dielectric value must be ≥ 1.

sdens

This keyword specifies the number of quadrature points per $Å^2$ to use in calculation surface terms (e.g., molecular surface, solvent accessible surface). This keyword is ignored when *srad* is 0.0 (e.g., for van der Waals surfaces) or when *srfm (elec)* is `spl2` (e.g., for spline surfaces). The syntax is:

```
sdens {density}
```

where `density` is a floating point number indicating the number of grid points per $Å^{-2}$. A typical value is 10.0.

Note: There is a strong correlation between the value used for the sphere density, the accuracy of the results, and the APBS calculation time.

sdie

Specify the dielectric constant of the solvent. The syntax is:

```
sdie {diel}
```

where `diel` is a floating point number representing the solvent dielectric constant (unitless). This number must be ≥ 1. Bulk water at biologically-relevant temperatures is usually modeled with a dielectric constant of 78-80.

srad

This keyword specifies the radius of the solvent molecules; this parameter is used to define various solvent-related surfaces and volumes (see *srfm (elec)*). This value is usually set to 1.4 Å for a water-like molecular surface and set to 0 Å for a van der Waals surface. The syntax is:

```
srad {radius}
```

where `radius` is the floating point value of the solvent radius (in Å). This keyword is ignored for `srfm spl2` (see *srfm (elec)*).

temp

This keyword specifies the temperature for the calculation. The syntax is:

```
temp {T}
```

where `T` is the floating point value of the temperature for calculation (in K).

tree_n0

TABI-PB parameter that specifies the maximum number of particles in a treecode leaf. This controls leaf size in the process of building the tree structure. The syntax is:

```
tree_n0 {max_number}
```

where `max_number` is an integer. A typical value for this parameter is 500.

tree_order

TABI-PB parameter that specifies the order of the treecode multipole expansion. The syntax is:

```
tree_order {order}
```

where `order` is an integer that indicates the Taylor expansion order. Users can adjust the order for different accuracy. A typical choice for this parameter is 3.

Background information

The Treecode-Accelerated Boundary Integral Poisson-Boltzmann solver (TABI-PB; Geng, 2013 calculates electrostatics of solvated biomolecules governed by the linearized Poisson-Boltzmann equation. It uses a well-posed boundary integral Poisson-Boltzmann formulation to ensure rapid convergence. In addition, a fast treecode algorithm for the screened Coulomb potential (Li, 2009) is applied to speed up the matrix-vector products in each GMRES iteration. The molecular surfaces, which divide the entire domain into solute region and solvent region, are generated by MSMS or NanoShaper.

TABI-PB algorithm

The coupled integral equations derived from the linearized Poisson-Boltzmann equation are

$$\frac{1}{2}(1+\epsilon)\phi(x) - \int_\Gamma (K_1(x,y)\frac{\partial\phi(y)}{\partial v} + K_2(x,y)\phi(y))dS_y = S_1(x)$$
$$\frac{1}{2}(1+\frac{1}{\epsilon})\frac{\partial\phi(x)}{\partial v} - \int_\Gamma (K_3(x,y)\frac{\partial\phi(y)}{\partial v} + K_4(x,y)\phi(y))dS_y = S_2(x), x \in \Gamma$$

for the surface potential ϕ, and its normal derivative $\frac{\partial\phi}{\partial v}$ on the surface :math‘Gamma‘. The kernels $K_{1,2,3,4}$ are linear combinations of the Coulomb and screened Coulomb potentials:

$$G_0(x,y) = \frac{1}{4\pi|x-y|}$$
$$G_\kappa(x,y) = \frac{e^{-\kappa|x-y|}}{4\pi|x-y|}$$

and their first and second derivatives.

The sums in the discretized form of the integral equations above have the form of *N*-body interactions,

$$V_i = \sum_{j=1,j\neq i}^{N} q_j G(x_i,x_j), i = 1,\ldots,N$$

where G is the screened Coulomb potential kernel, x_i, x_j are the centroids of the triangles, and q_j is the charge at x_j. The particles (centroids of the triangles) are divided into a hierarchy of clusters having a tree structure. The treecode replaces the $\mathcal{O}(N^2)$ particle-particle interactions by $\mathcal{O}(N\log N)$ particle-cluster interactions and TABI-PB utilizes this feature efficiently.

Output

The TABI-PB code produces an output file called `surface_potential.dat` containing:

- number of nodes, number of triangles
- node index, vertices, normal vector, surface potential (kJ mol^{-1} e_c^{-1}), surface potential normal derivatives (kJ mol^{-1} e_c^{-1} A^{-1})
- connectivity data for MSMS surface triangulation

The format is given below:

```
num_node num_triangle
node_index x y z norm_x norm_y norm_z phi norm_phi
(et cetera)
node_index1 node_index2 node_index3
```

The TABI-PB code prints the free energy of solvation and Coulombic free energy in kJ/mol, along with some other information such as CPU time and the GMRES residuals at each step.

Additionally, TABI-PB can optionally output a VTK polygonal data file containing color mappable potentials and normal derivatives of potentials on the faces and vertices of the mesh. The VTK file can be visualized using ParaView.

fe-manual

Manually-configured adaptive finite element Poisson-Boltzmann calculations.

This is a single-point PBE calculation performed by our adaptive finite element PBE solver. It requires that APBS be linked to the Michael Holst group FEtk finite element library during compilation. The finite element solver uses a "solve-estimate-refine" cycle. Specifically, starting from an initial mesh, it performs the following iteration:

1. solve the problem with the current mesh
2. estimate the error in the solution
3. adaptively refine the mesh to reduce the error

This iteration is repeated until a global error tolerance is reached.

Keywords for this calculation type include:

akeyPRE

Specifies how the initial finite element mesh should be constructed (from refinement of a very coarse 8-tetrahedron mesh prior to the solve-estimate-refine iteration in *fe-manual* finite element calculations. The syntax is:

```
akeyPRE {key}
```

where `key` is a text string that specifies the method used to guide initial refinement and takes one of the values:

`unif` Uniform refinement

`geom` Geometry-based refinement at molecular surfaces and charges

akeySOLVE

Specifies how the the finite element mesh should be adaptively subdivided during the solve-estimate-refine iterations of a *fe-manual* finite element calculation. The syntax is:

```
akeySOLVE {key}
```

where `key` is a text string that specifies the method used to guide adaptive refinement:

resi Residual-based a *posteriori* refinement.

bcfl

Specifies the type of boundary conditions used to solve the Poisson-Boltzmann equation. The syntax is:

```
bcfl {flag}
```

where `flag` is a text string that identifies the type of conditions to be used.

zero "Zero" boundary condition. Dirichlet conditions where the potential at the boundary is set to zero. This condition is not commonly used and can result in large errors if used inappropriately.

sdh "Single Debye-Hückel" boundary condition. Dirichlet condition where the potential at the boundary is set to the values prescribed by a Debye-Hückel model for a single sphere with a point charge, dipole, and quadrupole. The sphere radius in this model is set to the radius of the biomolecule and the sphere charge, dipole, and quadrupole are set to the total moments of the protein. This condition works best when the boundary is sufficiently far from the biomolecule.

mdh "Multiple Debye-Hückel" boundary condition. Dirichlet condition where the potential at the boundary is set to the values prescribed by a Debye-Hückel model for a multiple, non-interacting spheres with a point charges. The radii of the non-interacting spheres are set to the atomic radii of and the sphere charges are set to the atomic charges. This condition works better than sdh for closer boundaries but can be very slow for large biomolecules.

focus "Focusing" boundary condition. Dirichlet condition where the potential at the boundary is set to the values computed by the previous (usually lower-resolution) PB calculation. This is **only** used in sequential focusing performed manually in *mg-manual* calculations. All of the boundary points should lie within the domain of the previous calculation for best accuracy; if any boundary points lie outside, their values are computed using single Debye-Hückel boundary conditions (see above).

map Specifying map allows a previously calculated potential map to be used in a new focusing calculation. A typical scenario is using the same coarse grid for multiple focusing calculations. A potential map can be written once from a coarse grid calculation, then used in subsequent runs to bypass the need to recalculate the coarse grid. See the READ keyword pot (see *READ input file section*) and the attached example files for its use.

calcenergy

This optional keyword controls energy output from an apolar solvation calculation. The syntax is:

```
calcenergy <flag>
```

where `flag` is a string denoting what type of energy to calculate:

no (Deprecated) Don't calculate any energies.

total Calculate and return total apolar energy for the entire molecule.

comps Calculate and return total apolar energy for the entire molecule as well as the energy components for each atom.

Note: This option must be used consistently (with the same `flag` value) for all calculations that will appear in subsequent *PRINT input file section* statements.

calcforce

This optional keyword controls energy output from an apolar solvation calculation. The syntax is:

```
calcforce {flag}
```

where `flag` is a text string that specifies the types of force values to be returned:

no (Deprecated) don't calculate any forces.

total Calculate and return total electrostatic and apolar forces for the entire molecule.

comps Calculate and return total electrostatic and apolar forces for the entire molecule as well as force components for each atom.

The possible outputs from calcforce are:

tot {n} total force for atom *n*

qf {n} fixed charge force for atom *n*

db {n} dielectric boundary force for atom *n*

ib {n} ionic boundary force for atom *n*

The values will be printed in three columns which correspond to the x, y, and z components of the force vector.

Note: This option must be used consistently (with the same `flag` value) for all calculations that will appear in subsequent *PRINT input file section* statements.

chgm

Specify the method by which the biomolecular point charges (i.e., Dirac delta functions) by which charges are mapped to the grid for a multigrid (*mg-manual*, *mg-auto*, *mg-para*) Poisson-Boltzmann calculation. As we are attempting to model delta functions, the support (domain) of these discretized charge distributions is always strongly dependent on the grid spacing. The syntax is:

```
chgm {flag}
```

`flag` is a text string that specifies the type of discretization:

spl0 Traditional trilinear interpolation (linear splines). The charge is mapped onto the nearest-neighbor grid points. Resulting potentials are very sensitive to grid spacing, length, and position.

spl2 Cubic B-spline discretization. The charge is mapped onto the nearest- and next-nearest-neighbor grid points. Resulting potentials are somewhat less sensitive (than `spl0`) to grid spacing, length, and position.

spl4 Quintic B-spline discretization. Similar to `spl2`, except the charge/multipole is additionally mapped to include next-next-nearest neighbors (125 grid points receive charge density).

domainLength

Specify the rectangular finite element mesh domain lengths for *fe-manual* finite element calculations. This length may be different in each direction. If the *usemesh* keyword is included, then this command is ignored. The syntax is:

```
domainLength {xlen ylen zlen}
```

where the parameters `xlen ylen zlen` are floating point numbers that specify the mesh lengths in the x-, y-, and z-directions (respectively) in units of Å.

ekey

Specify the method used to determine the error tolerance in the solve-estimate-refine iterations of the finite element solver (*fe-manual*). The syntax is:

```
ekey { flag }
```

where `flag` is a text string that determines the method for error calculation.

`simp` Per-simplex error limit

`global` Global (whole domain) error limit

`frac` Fraction of simplices you'd like to see refined at each iteration

etol

Specifies the tolerance for iterations of the partial differntial equation solvers: The syntax is:

```
etol { tol }
```

where `tol` is the (floating point) numerical value for the error tolerance.

For finite difference solvers, this keyword is optional and is intended for *mg-manual*, *mg-auto*, and *mg-para* calculation types.

For finite element solvers, this keyword specifies the tolerance for error-based adaptive refinement during the solve-estimate-refine iterations of the finite element solver (*fe-manual*), where `tol` is the (floating point) numerical value for the error tolerance.

lpbe

Specifies that the linearized Poisson-Boltzmann equation should be solved.

Note: The options *lpbe*, *npbe*, *lrpbe*, *nrpbe* are mutually exclusive.

lrpbe

Specifies that the linear form of the regularized Poisson-Boltzmann equation (RPBE) should be solved. The regularized PBE equation replaces the point charge distribution with the corresponding Green's function. As a result of this replacement, the solution corresponds to the reaction field instead of the total potential; the total potential can be

recovered by adding the appropriate Coulombic terms to the solution. Likewise, this equation immediately yields the solvation energy without the need for reference calculations.

Note: The options *lpbe*, *npbe*, *lrpbe*, *nrpbe* are mutually exclusive.

maxsolve

Specify the number of times to perform the solve-estimate-refine iteration of the finite element solver (*fe-manual*). The syntax is:

```
maxsolve { num }
```

where *num* is an integer indicating the desired maximum number of iterations.

maxvert

Specify the maximum number of vertices to allow during solve-estimate-refine cycle of finite element solver (*fe-manual*). This places a limit on the memory that can be used by the solver. The syntax is:

```
maxvert { num }
```

where `num` is an integer indicating the maximum number of vertices.

npbe

Specifies that the nonlinear (full) Poisson-Boltzmann equation should be solved.

Note: The options *lpbe*, *npbe*, *lrpbe*, *nrpbe* are mutually exclusive.

nrpbe

Specifies that the nonlinear form of the regularized Poisson-Boltzmann equation (RPBE) should be solved. The regularized PBE equation replaces the point charge distribution with the corresponding Green's function. As a result of this replacement, the solution corresponds to the reaction field instead of the total potential; the total potential can be recovered by adding the appropriate Coulombic terms to the solution. Likewise, this equation immediately yields the solvation energy without the need for reference calculations.

Note: The options *lpbe*, *npbe*, *lrpbe*, *nrpbe* are mutually exclusive.

Note: This functionality is only available with FEM-based solvers.

srfm (elec)

Specify the model used to construct the dielectric and ion-accessibility coefficients. The syntax for this command is:

```
srfm {flag}
```

where `flag` is a string describing the coefficient model:

mol The dielectric coefficient is defined based on a molecular surface definition. The problem domain is divided into two spaces. The "free volume" space is defined by the union of solvent-sized spheres (see *srad*) which do not overlap with biomolecular atoms. This free volume is assigned bulk solvent dielectric values. The complement of this space is assigned biomolecular dielectric values. With a non-zero solvent radius (srad), this choice of coefficient corresponds to the traditional definition used for PB calculations. When the solvent radius is set to zero, this corresponds to a van der Waals surface definition. The ion-accessibility coefficient is defined by an "inflated" van der Waals model. Specifically, the radius of each biomolecular atom is increased by the radius of the ion species (as specified with the *ion* keyword). The problem domain is then divided into two spaces. The space inside the union of these inflated atomic spheres is assigned an ion-accessibility value of 0; the complement space is assigned bulk ion accessibility values.

smol The dielectric and ion-accessibility coefficients are defined as for mol (see above). However, they are then "smoothed" by a 9-point harmonic averaging to somewhat reduce sensitivity to the grid setup as described by Bruccoleri et al. J Comput Chem 18 268-276, 1997 (10.1007/s00214-007-0397-0).

spl2 The dielectric and ion-accessibility coefficients are defined by a cubic-spline surface as described by Im et al, Comp Phys Commun 111 (1-3) 59-75, 1998 (10.1016/S0010-4655(98)00016-2). The width of the dielectric interface is controlled by the *swin* parameter. These spline-based surface definitions are very stable with respect to grid parameters and therefore ideal for calculating forces. However, they require substantial reparameterization of the force field; interested users should consult Nina et al, Biophys Chem 78 (1-2) 89-96, 1999 (10.1016/S0301-4622(98)00236-1). Additionally, these surfaces can generate unphysical results with non-zero ionic strengths; this is an on-going area of development.

spl4 The dielectric and ion-accessibility coefficients are defined by a 7th order polynomial. This surface definition has characteristics similar to spl2, but provides higher order continuity necessary for stable force calculations with atomic multipole force fields (up to quadrupole).

swin

Specify the size of the support (i.e., the rate of change) for spline-based surface definitions (see *srfm (elec)*). The syntax is:

```
swin {win}
```

where `win` is a floating point number for the spline window width (in Å). Usually 0.3 Å.</p> Note that, per the analysis of Nina, Im, and Roux (article), the force field parameters (radii) generally need to be adjusted if the spline window is changed.

targetNum

Specify the target number of vertices in the initial finite element mesh for *fe-manual* calculations. The syntax is:

```
targetNum { num }
```

where `num` is an integer denoting the target number of vertices in initial mesh. Initial refinement will continue until this number is reached or the the longest edge of every simplex is below *targetRes*.

targetRes

Specify the target resolution of the simplices in a finite element mesh (*fe-manual*). The syntax is:

```
targetRes { res }
```

where `res` is a floating point number denoting the target resolution for longest edges of simplices in mesh (in Å). Refinement will continue until the longest edge of every simplex is below this value or the number of vertices reaches *targetNum*.

usemesh

Specify the external finite element mesh to be used in the finite element Poisson-Boltzmann calculation (*fe-manual*). These must have been input via an earlier READ mesh statement (see *READ input file section*). The syntax is:

```
usemesh {id}
```

where `id` is an integer ID specifying the particular map read in with *READ input file section*. These IDs are assigned sequentially, starting from 1, and incremented independently for each mesh read by APBS.

write

This controls the output of scalar data calculated during the Poisson-Boltzmann run. This keyword can be repeated several times to provide various types of data output from APBS. The syntax is:

```
write {type} {format} {stem}
```

type A string indicating what type of data to output:</p>

charge Write out the biomolecular charge distribution in units of e_c (electron charge) per $Å^3$ (multigrid only).

pot Write out the electrostatic potential over the entire problem domain in units of k_b T e_c^{-1} (multigrid and finite element), where

k_b Boltzmann's constant: 1.3806504×10^{23} J K^{-1}

T The temperature of your calculation in K

e_c is the charge of an electron: $1.60217646 \times 10^{-19}$ C

As an example, if you ran your calculation at 300 K, then the potential would be written out as multiples of k_b T e_c^{-1} = (1.3806504×10^{23} J K^{-1}) × (300 K) × ($1.60217646 \times 10^{-19}$ C)$^{-1}$ = ($4.1419512 \times 10^{-21}$ J) × ($6.241509752 \times 10^{18}$ C^{-1}) = 25.85202 mV

atompot Write out the electrostatic potential at each atom location in units of k_b T e_c^{-1} (multigrid and finite element).

smol Write out the solvent accessibility defined by the molecular surface definition (see *srfm (elec)* `smol`). Values are unitless and range from 0 (inaccessible) to 1 (accessible). (multigrid and finite element).

sspl Write out the spline-based solvent accessibility (see *srfm (elec)* `spl2`). Values are unitless and range from 0 (inaccessible) to 1 (accessible) (multigrid and finite element)

vdw Write out the van der Waals-based solvent accessibility (see *srfm (elec)* `smol` with *srad* 0.0). Values are unitless and range from 0 (inaccessible) to 1 (accessible). (multigrid and finite element)

ivdw Write out the inflated van der Waals-based ion accessibility (see *srfm (elec)* `smol`). Values are unitless and range from 0 (inaccessible) to 1 (accessible). (multigrid and finite element)

lap Write out the Laplacian of the potential $\nabla^2\phi$ in units of k_B T e_c^{-1} Å^{-2} (multigrid only).

edens Write out the "energy density" $-\nabla \cdot \epsilon\nabla\phi$ in units of k_B T e_c^{-1} Å^{-2} (multigrid only).

ndens Write out the total mobile ion number density for all ion species in units of M (multigrid only). The output is calculated according to the formula (for nonlinear PB calculations): $\rho(x) = \sum_i^N \bar{\rho}_i e^{-q_i\phi(x)-V_i(x)}$, where *N* is the number of ion species, $\bar{\rho}_i$ is the bulk density of ion species *i*, q_i is the charge of ion species *i*, $\phi(x)$ is the electrostatic potential, and V_i is the solute-ion interaction potential for species *i*.

qdens Write out the total mobile ion charge density for all ion species in units of e_c M (multigrid only). The output is calculated according to the formula (for nonlinear PB calculations): $\rho(x) = \sum_i^N \bar{\rho}_i q_i e^{-q_i\phi(x)-V_i(x)}$, where *N* is the number of ion species, $\bar{\rho}_i$ is the bulk density of ion species *i*, q_i is the charge of ion species *i*, $\phi(x)$ is the electrostatic potential, and V_i is the solute-ion interaction potential for species *i*.

dielx or diely or dielz Write out the dielectric map shifted by 1/2 grid spacing in the {x, y, z}-direction (see *READ input file section* `diel`). The values are unitless (multigrid only).

format A string that specifies the format for writing out the data:

dx Write out data in *OpenDX scalar data format*. This is the preferred format for APBS I/O. (multigrid and finite element).

avs Write out data in AVS UCD format. (finite element only).

uhbd Write out data in *UHBD scalar data format*. (multigrid only).

gz Write out *OpenDX scalar data format* in gzipped (zlib) compatible format. Appends .dx.gz to the filename.

flat Write out data as a plain text file. (multigrid and finite element).

stem A string that specifies the path for the output; files are written to `stem.XYZ`, where `XYZ` is determined by the file format (and processor rank for parallel calculations). If the pathname contains spaces, then it must be surrounded by double quotes.

Note: The finite element methods are currently most useful for a select set of problems which can benefit from adaptive refinement of the solution. Furthermore, this implementation is experimental. In general, the sequential and parallel focusing multigrid methods offer the most efficient solution of the PBE for most systems.

---

geoflow-auto

To increase the accuracy of our implicit solvent modeling, we have implemented a differential geometry based geometric flow solvation model (Thomas, 2013). In this model, polar and nonpolar solvation free energies are coupled and the solvent-solute boundary is determined in a self-consistent manner. Relevant references are provided in *Recommended reading*. This section provides a brief overview of the method.

The solutions for the electrostatic potential ϕ and the characteristic function S (related to the solvent density) are obtained by minimizing a free energy functional that includes both polar and nonpolar solvation energy terms. Minimization of the functional with respect to ϕ gives the Poisson-Boltzmann equation with a dielectric coefficient ϵ has the solute value ϵ_m where $S = 1$ and the solvent value ϵ_s where $S = 0$. Minimization of the free energy functional with respect to S gives

$$-\nabla \cdot \left(\gamma \frac{\nabla S}{\parallel \nabla S \parallel}\right) + p - \rho_0 U^{att} + \rho_m \phi - \frac{1}{2}\epsilon_m \mid \nabla\phi \mid^2 + \frac{1}{2}\epsilon_s \mid \nabla\phi \mid^2 = 0$$

where γ is the microscopic surface tension, p is the hydrostatic pressure, and U^{att} is the attractive portion of the van der Waals dispersion interaction between the solute and the solvent.

Keywords for this calculation type include:

bconc

This keyword specifies the bulk solvent density. This coefficient multiplies the integral term of the apolar model discussed above and can be set to zero to eliminate integral contributions to the apolar solvation calculation. The syntax is:

```
bconc <density>
```

where `density` is a floating point number giving the bulk solvent density in $Å^{-3}$.

gamma

This keyword specifies the surface tension coefficient for apolar solvation models.

```
gamma { value }
```

where `value` is a floating point number designating the surface tension in units of kcal mol^{-1} $Å^{-2}$. This term can be set to zero to eliminate the SASA (solvent-accessible surface area) contributions to the apolar solvation calculations.

Warning: *Either* this documentation is incorrect *or* the implementation needs to be changed to use kJ mol^{-1} $Å^{-2}$ instead of kcal.

Todo

Resolve unit confusion with geometric flow *gamma* keyword. https://github.com/Electrostatics/apbs-pdb2pqr/issues/490

press

This term specifies the solvent pressure in kJ mol^{-1} $Å^{-3}$. This coefficient multiplies the volume term of the apolar model and can be set to zero to eliminate volume contributions to the apolar solvation calculation. The syntax is:

```
press {value}
```

where `value` is the floating point value of the pressure coefficient in kJ mol^{-1} $Å^{-3}$.

Warning: *Either* this documentation is incorrect *or* the implementation needs to be changed to use kJ mol^{-1} $Å^{-3}$ instead of kcal.

Todo

Resolve unit confusion with geometric flow `press` keyword and the apolar *press* keyword. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/499

vdwdisp

Specify whether the attractive van der Waals contribution to the geometric flow potential is on or off.

```
vdwdisp { flag }
```

where `flag` is 0 (vdw off) or 1 (vdw on).

Warning: Although the `ion` and `lpbe` keywords will be accepted in the geoflow-auto calculation, the treatment of salt is not currently implemented in APBS geometric flow.

Todo

Add LPBE/NPBE support to geometric flow or remove the `ion` and `lpbe` keywords. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/491

Todo

If there's only one mode, then we can change the keyword from `geoflow-auto` to just `geoflow`. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/492

mg-auto

Automatically configured finite difference Poisson-Boltzmann calculations.

This multigrid calculation automatically sets up and performs a string of single-point PBE calculations to "focus" on a region of interest (binding site, etc.) in a system. It is basically an automated version of *mg-manual* designed for easier use. Most users should use this version of ELEC.

Focusing is a method for solving the Poisson-Boltzmann equation in a finite difference setting. Some of the earliest references to this method are from Gilson and Honig[1]. The method starts by solving the equation on a coarse grid (i.e., few grid points) with large dimensions (i.e., grid lengths). The solution on this coarse grid is then used to set the Dirichlet boundary condition values for a smaller problem domain – and therefore a finer grid – surrounding the region of interest. The finer grid spacing in the smaller problem domain often provides greater accuracy in the solution.

The following keywords are present in mg-auto ELEC blocks; all keywords are required unless otherwise noted.

Note: During focusing calculations, you may encounter the message "WARNING! Unusually large potential values detected on the focusing boundary!" for some highly charged systems based on location of the focusing boundary. First, you should determine if you received any other warning or error messages as part of this calculation, particularly those referring to exceeded number of iterations or error tolerance (*etol*). Next, you should check if the calculation converged to a reasonable answer. In particular, you should check sensitivity to the grid spacing by making small changes to the grid lengths (via the *fglen* parameter) and see if the changes in energies are correspondingly small. If so, then this warning can be safely ignored.

[1] Gilson MK and Honig BH, Calculation of electrostatic potentials in an enzyme active site. Nature, 1987. 330(6143): p. 84-6. DOI:10.1038/330084a0

cgcent

This keyword controls electrostatic energy output from a Poisson-Boltzmann calculation The syntax is:

```
cgcent { mol id | xcent ycent zcent }
```

The arguments for this keyword are **either**

mol id Center the grid on molecule with integer ID `id`; as assigned in the `READ` section with a `READ mol` command (see *READ input file section*)

or

xcent ycent zcent Center the grid on the (floating point) coordinates (in Å) at which the grid is centered. Based on the PDB coordinate frame.

cglen

Specify the length of the coarse grid (in a focusing calculation) for an automatic multigrid (*mg-auto*, *mg-para*) Poisson-Boltzmann calculation. This may be different in each direction.

```
cglen {xlen ylen zlen}
```

This is the starting mesh, so it should be large enough to complete enclose the biomolecule and ensure that the chosen boundary condition (see *bcfl*) is appropriate.

xlen ylen zlen Grid lengths (floating point numbers) in the x-, y-, and z-directions in Å.

dime

Specifies the number of grid points per processor for grid-based discretization. The syntax is:

```
dime {nx ny nz}
```

For *mg-manual* calculations, the arguments are dependent on the choice of *nlev* by the formula: $n = c2^{l+1} + 1$ where n is the dime argument, c is a non-zero integer, l is the *nlev* value. The most common values for grid dimensions are 65, 97, 129, and 161 (they can be different in each direction); these are all compatible with a *nlev* value of 4. If you happen to pick a "bad" value for the dimensions (i.e., mismatch with *nlev*), the APBS code will adjust the specified *dime* downwards to more appropriate values. This means that "bad" values will typically result in lower resolution/accuracy calculations! The arguments for this keyword are:

nx ny nz The (integer) number of grid points in the x-, y-, and z-directions, respectively.

Note: dime should be interpreted as the number of grid points per processor for all calculations, including *mg-para*. This interpretation helps manage the amount of memory per-processor - generally the limiting resource for most calculations.

---

fgcent

Specify the center of the fine grid (in a focusing calculation) based on a molecule's center or absolute coordinates for *mg-para* and *mg-auto* multigrid calculations. The syntax is:

where a user can specify **either**

mol {id} Center the grid on molecule with integer ID id; as assigned in the READ section (see *READ input file section*) of the input file. Molecule IDs are assigned in the order they are read, starting at 1.

or the user can specify

xcent ycent zcent Center the grids on the coordinates (floating point numbers in Å) at which the grid is centered. Based on the input molecule PDB coordinate frame.

fglen

Specifies the fine mesh domain lengths in a multigrid focusing calculation (*mg-para* or *mg-auto*); this may be different in each direction. The syntax is:

```
fglen {xlen ylen zlen}
```

This should enclose the region of interest in the molecule. The arguments to this command are:

xlen ylen zlen Grid lengths (floating point numbers) in the x-, y-, and z-directions in Å.

usemap

Specify pre-calculated coefficient maps to be used in the Poisson-Boltzmann calculation. These must have been input via an earlier READ statement (see *READ input file section*).

The syntax for this command is:

```
usemap {type} {id}
```

where the mandatory keywords are:

type A string that specifies the type of pre-calculated map to be read in:

diel Dielectric function map (as read by *READ input file section* `diel`); this causes the *pdie*, *sdie*, *srad*, *swin*, and *srfm (elec)* parameters and the radii of the biomolecular atoms to be ignored when computing dielectric maps for the Poisson-Boltzmann equation. Note that the *pdie* and *sdie* values are still used for some boundary condition calculations as specified by *bcfl*.

kappa Mobile ion-accessibility function map (as read by *READ input file section* `kappa`); this causes the *swin* and *srfm (elec)* parameters and the radii of the biomolecular atoms to be ignored when computing mobile ion values for the Poisson-Boltzmann equation. The *ion* parameter is not ignored and will still be used.

charge Charge distribution map (as read by *READ input file section* `charge`); this causes the *chgm* parameter and the charges of the biomolecular atoms to be ignored when assembling the fixed charge distribution for the Poisson-Boltzmann equation.

pot Potential map (as read by *READ input file section* `pot`); this option requires setting *bcfl* to `map`.

id As described in the READ command documentation (see *READ input file section*), this integer ID specifies the particular map read in with READ. These IDs are assigned sequentially, starting from 1, and incremented independently for each map type read by APBS. In other words, a calculation that uses two PQR files, one parameter file, three charge maps, and four dielectric maps would have PQR files with IDs 1-2, a parameter file with ID 1, charge maps with IDs 1-3, and dielectric maps with IDs 1-4.

writemat

This controls the output of the mathematical operators in the Poisson-Boltzmann equation as matrices in Harwell-Boeing matrix format (multigrid only). The syntax is:

```
writemat {type} {stem}
```

where

type A string that indicates what type of operator to output.

poisson Write out the Poisson operator $-\nabla \cdot \epsilon \nabla$.

stem A string that specifies the path for the output.

mg-manual

Manually-configured finite differnece multigrid Poisson-Boltzmann calculations.

This is a standard single-point multigrid PBE calculation without focusing or additional refinement. The `mg-manual` calculation offers the most control of parameters to the user. Several of these calculations can be strung together to perform focusing calculations by judicious choice of the *bcfl* flag; however, the setup of the focusing is not automated as it is in *mg-auto* and *mg-para* calculations and therefore this command should primarily be used by more experienced users.

gcent

Specify the center of the grid based on a molecule's center or absolute coordinates *mg-manual* multigrid calculations. The syntax is:

```
fgcent { mol id | xcent ycent zcent }
```

where a user can specify **either**

mol {id} Center the grid on molecule with integer ID id; as assigned in the READ section (see *READ input file section*) of the input file. Molecule IDs are assigned in the order they are read, starting at 1.

or the user can specify

xcent ycent zcent Center the grids on the coordinates (floating point numbers in Å) at which the grid is centered. Based on the input molecule PDB coordinate frame.

glen

Specify the mesh domain lengths for multigrid *mg-manual* calculations. These lengths may be different in each direction. The syntax is:

```
glen {xlen ylen zlen}
```

where `xlen ylen zlen are the (floating point) grid lengths in the x-, y-, and z-directions (respectively) in Å.

grid

Specify the grid spacings for multigrid and volume integral calculations. This value may be different in each direction. The syntax is:

```
grid {hx hy hz}
```

where `hx hy hz` are the (floating point) grid spacings in the x-, y-, and z-directions (respectively) in Å.

nlev

Specify the depth of the multilevel hierarchy used in the *mg-manual* multigrid solver. See *dime* for a discussion of how nlev relates to grid dimensions. The syntax is:

```
nlev {lev}
```

where `lev` is an integer indicating the desired depth of the multigrid hierarchy.

mg-para

Automatically-configured parallel focusing multigrid Poisson-Boltzmann calculations.

This calculation closely resembles *mg-auto* in syntax. However, it is designed to perform electrostatics calculations on systems in a parallel focusing fashion.

async

An optional keyword to perform an asynchronous parallel focusing Poisson-Boltzmann equation. The syntax is

```
async {rank}
```

where `rank` is the integer ID of the particular processor to masquerade as. Processor IDs range from *0* to *N-1*, where *N* is the total number of processors in the run (see *pdime*). Processor IDs are related to their position in the overall grid by $p = nxnyk + nxj + i$ where nx is the number of processors in the x-direction, ny is the number of processors in the y-direction, nz is the number of processors in the z-direction, i is the index of the processor in the x-direction, j is the index of the processor in the y-direction, k is the index of the processor in the z-direction, and p is the overall rank of the processor.

ofrac

Specify the amount of overlap to include between the individual processors meshes in a parallel focusing calculation (*mg-para*). The syntax is:

```
ofrac {frac}
```

where `frac` is a floating point value between 0.0 and 1.0 denoting the amount of overlap between processors. Empirical evidence suggests that an value of 0.1 is sufficient to generate stable energies. However, this value may not be sufficient to generate stable forces and/or good quality isocontours. For example, the following table illustrates the change in energies and visual artifacts in isocontours as a function of ofrac values for a small peptide (2PHK:B).

Table 6.1: Sensitivity of 2PHK:B solvation energy calculations to ofrac values.

`ofrac` value	Energy (kJ/mol)	Visual artifact in isocontour?
0.05	342.79	No
0.06	342.00	No
0.07	341.12	Yes
0.08	341.14	Yes
0.09	342.02	Yes
0.10	340.84	Yes
0.11	339.67	No
0.12	341.10	No
0.13	341.10	No
0.14	341.32	No
0.15	341.54	No

In general, larger <code>ofrac</code> values will reduce the parallel efficiency but will improve the accuracy.

For broad spatial support of the splines, every charge included in partition needs to be at least 1 grid space (*chgm* `spl0`), 2 grid spaces (*chgm* `spl2`), or 3 grid spaces (*chgm* `spl4`) away from the partition boundary.

pdime

Specify the processor array to be used in a parallel focusing (*mg-para*) calculation. The syntax is:

```
pdime {npx npy npz}
```

where `npx npy npz` are the integer number of processors to be used in the x-, y- and z-directions of the system. The product `npx × npy × npz` should be less than or equal to the total number of processors with which APBS was invoked (usually via mpirun). If more processors are provided at invocation than actually used during the run, the extra processors are not used in the calculation. The processors are tiled across the domain in a Cartesian fashion with a specified amount of overlap (see *ofrac*) between each processor to ensure continuity of the solution. Each processor's subdomain will contain the number of grid points specified by the dime keyword. For broad spatial support of the splines, every charge included in partition needs to be at least 1 grid space (*chgm* `spl0`), 2 grid spaces (*chgm* `spl2`), or 3 grid spaces (*chgm* `spl4`) away from the partition boundary.

mg-dummy

Not a Poisson-Boltzmann calculation. Many calculations of surface and charge distribution properties which do not require solution of the PBE.

This type of calculation allows users to write out dielectric, ion-accessibility, and charge distribution, and other types of maps that depend solely on biomolecular geometry. Since these maps depend only on geometry, they can be written out without actually solving the PB equation.

pbam-auto

PB-AM is an analytical solution to the linearized Poisson-Boltzmann equation for multiple spherical objects of arbitrary charge distribution in an ionic solution. More details on the method are available in Lotan, Head-Gordon (2006). The physical calculations are uses to perform various actions on a system of molecules such as calculation of energies, forces, torques, electrostatic potentials, and Brownian dynamics schemes. This fast method coarse-grains all molecules of the system into single spheres large enough to contain all molecule atoms.

Todo

If there's only one mode to PBAM, let's call it `pbam` instead of `pbam-auto`. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/498

The current implementation of PB-AM in APBS includes:

- Calculation of energies, forces and torques
- Calculation of electrostatic potentials
- Brownian dynamics simulations

Keywords for this calculation type include:

3dmap

Specify the name of the file into which the potential surface on the coarse-grain molecule surface will be printed.

```
3dmap {filename}
```

where `filename` is a string for the name of the file where a 3D grid will be printed out.

Todo

The PB-(S)AM `3dmap` keyword should not exist; please replace it ASAP with the *write* command. Documented this todo as https://github.com/Electrostatics/apbs-pdb2pqr/issues/482

diff

Specify the diffusion coefficients for each molecule in the system for a PB-(S)AM Brownian dynamics calculation.

```
diff {type} {dTrans} {dRot}
```

type a string indicating the molecule dynamics type

stat Stationary.

rot Object is fixed but rotates

move Object moves and rotates.

dTrans Translational diffusion coefficient in units of $Å^2$ ps^{-1}. Used only with the `move` keyword.

dRot Rotational diffusion coefficient. Used with the `move` and `rot` keywords.

Todo

What are the units for `dRot`? Documented as https://github.com/Electrostatics/apbs-pdb2pqr/issues/486

Note: The order of these keywords is expected to be identical to the order of the molecules in the READ section.

Todo

Add a `mol id` flag rather than have an implicit ordering of the `diff` keywords. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/487

dx

Specify the name of the file into which the potential will be printed.

```
dx {filename}
```

where `filename` is a string for the name of the file where an OpenDX file will be printed out.

Todo

The PB-(S)AM `dx` keyword should not exist; please replace it ASAP with the *write* command. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/488

grid2d

Specify the filename and location of a 2D cross sectional potential to be written to.

```
grid2d {filename} {axis} {axis_value}
```

`filename` String for the name of the 2D grid to be printed out

`axis` String of either x, y, or z, for which cartesian axis the grid will be computed along

`axis_value` A floating point number of the position along <code>axis</code> that will be used.

Note: Multiple 2D files can be printed out with 1 PB-AM run. Just specify them with more grid2d flags.

Todo

The PB-(S)AM `grid2d` keyword should not exist; please replace it ASAP with the *write* command. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/493

gridpts

Specify the number of gridpoints in each cartesian dimension.

```
gridpts {pts}
```

where `pts` is a integer number indicating the number of grid points.

Todo

The PB-(S)AM `gridpts` keyword should not exist; it's duplicative of the existing *dime* keyword! Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/494

ntraj

Specify the number of Brownian Dynamic trajectories desired for the PB-(S)AM run.

```
ntraj {traj}
```

where `traj` is an integer of the number of desired trajectories.

pbc

This keyword is used to indicate if 3D periodic boundary conditions (PBCs) will be used in a PB-(S)AM calculation. If used, a box length must also be specified, in Ångstroms.

```
pbc {boxlength}
```

where `boxlength` is the floating point value of the box length in Ångstroms.

Note: The box is centered at the origin (0, 0, 0). The code assumes a minimum image convention, so it only includes the closest image of the neighboring molecules. For this convention to always be preserved, the periodic box is assumed to be large enough such that the electrostatic forces are sufficiently attenuated beyond one boxlength. Generally, the program assumes a mutual polarization cutoff of 100 Å for the mutual polarization, so if the boxlength is shorter, the cutoff will be reduced to boxlength/2.

randorient

Flag to indicate that the molecules should have a random orientation in subsequent PB-(S)AM calculations.

runname

Specify the output name for the PB-(S)AM calculation.

..code-block:: bash

    runname {name}

where `name` is a string indicating the prefix for all PB-(S)AM output files.

runtype

Indicate what type of calculation you would like to run with the PB-(S)AM model.

```
runtype {type}
```

where `type` is the type of calculation to be perfomed:

`energyforce` Compute and print out the interaction energies, forces and torques on each molecule.

electrostatics Print the electrostatic potential of points in the system.

dynamics Perform a Brownian Dynamics simulation, using forces and torques generated from the PB-(S)AM model. The calculation of force and torque has been integrated into a Brownian dynamics scheme that is detailed in Yap EH, Head-Gordon TL (2013) This option will generate a series of files of the form

dyn_*toy*.pqr The starting configuration of the system for the first trajectory

dyn_*toy*.stat A file that prints how each trajectory was terminated and the time that this occurred at.

dyn_*toy*_traj.xyz A VMD-readable xyz file for the trajectory of `traj`.

dyn_toy_traj.dat A file with positions, forces and torques for the system.

Todo

The dynamics part of the PB-(S)AM code should be moved out of the `ELEC` section. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/500

---

salt

Specify the monovalent salt concentration of the system, in molar. This is usually a value between 0.00 to 0.15.

```
salt {saltConc}
```

where `saltConc` is the floating point value of the monovalent salt concentration in molar.

Todo

The PB-(S)AM `salt` keyword should be eradicated and replaced with the *ion* keyword. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/501

---

term

Specify a termination condition for a PB-(S)AM Brownian dynamics trajectory. The syntax is:

```
term {type} {options}
```

where the `options` are determined by the `type` as follows:

contact {file} Termination based on molecular contact conditions. `file` is a string for the contact file filename. The contact file has a list formatted as follows: `moltype1 at1 moltype2 at2 dist` where `moltype1` and `moltype2` are indices of the molecular types, `at1` is the index of an atom from the first molecular type, `at2` is the index of an atom from the second molecular type, and `dist` is the maximum distance between the two atoms that defines the contact. `pad` is distance criterion that will be checked in the case that the true atom contact distance may not be fulfilled.

Note: Sometimes these distances cannot be reached due to the assumption in this model that the molecule is spherical. If this is the case, the atom positions are transformed to the molecule surface and surface points are compared to the pad distance.

{pos} {val} {molecule} Specify a position termination condition for a given molecule. where `pos` is one of the following options: `x<=, x>=, y<=, y>=, z<=, z>=, r<=, r>=`. `val` is the value along the given axis to check against. `molecule` is the molecule index (1 based) according to the order of molecules listed in the `READ` section that this condition applies to. This command can be understood as: "Terminate the simulation when molecule `molecule` fulfills the condition `pos val`".

Todo

Add a constant keyword (e.g., like `position`) before the `{pos}` argument of `term`. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/503

time {val} Specify a time termination condition where `val` is a floating point number for the trajectory time limit (in picoseconds).

termcombine

Combine multiple PB-(S)AM Brownian dynamics trajectory termination conditions (see *term*) via logic operators

```
termcombine {op}
```

where `op` is either the string `or` or `and`. If `and` is selected, all listed termination conditions must be fulfilled before the simulation ends. If `or` is selected, only one needs to be satisfied to complete the simulation.

units

Specify the units for energy/force/potential output in PB-(S)AM calculations:

```
units {flag}
```

where `flag` specifies the unit system:

kcalmol kcal/mol

jmol J/mol

kT kT

Force units will be energy units/Angstrom and potential units will be energy units/electron.

Todo

It would be great to use the same units everywhere in APBS. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/485

xyz

For each molecule in the system and for each trajectory, specify a xyz file for the starting position of that molecule. The syntax is:

```
xyz {molecule_id} {filename}
```

molecule_id An integer (starting at 1) of the molecule index from the READ section

filename The name of the file for the xyz coordinates of the molecule center for a given trajectory. The trajectories for a given molecule should be ordered sequentially in the ELEC section. </p>

Todo

It would be nice to incorporate the `xyz` functionality into the *READ input file section* block. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/505

Background information

PB-AM is an analytical solution to the linearized Poisson-Boltzmann equation for multiple spherical objects of arbitrary charge distribution in an ionic solution. The solution can be reduced to a simple system of equations as follows:

$$A = \Gamma \cdot (\Delta \cdot T \cdot A + E)$$

Where $A^{(i)}$ represents the effective multipole expansion of the charge distributions of molecule i. $E^{(i)}$ is the free charge distribution of molecule i. Γ is a dielectric boundary-crossing operator, Δ is a cavity polarization operator, T an operator that transforms the multipole expansion to a local coordinate frame. $A^{(i)}$ is solved for through an iterative SCF method.

From the above formulation, computation of the interaction energy $\Omega^{(i)}$ for molecule i, is given as follows:

$$\Omega^{(i)} = \frac{1}{\epsilon_s} \left\langle \sum_{j \neq i}^{N} T \cdot A^{(j)}, A^{(i)} \right\rangle$$

where $\langle M, N \rangle$ denotes the inner product. Forces can be obtained from

$$\mathbf{F}^{(i)} = \nabla_i \Omega^{(i)} = \frac{1}{\epsilon_s} \left[\langle \nabla_i T \cdot A^{(i)}, A^{(i)} \rangle + \langle T \cdot A^{(i)}, \nabla_i A^{(i)} \rangle \right]$$

pbsam-auto

PB-SAM is a semi-analytical solution to the linearized Poisson-Boltzmann equation for multiple molecules of arbitrary charge distribution in an ionic solution. The solution is an extension of the *analytical method*, leveraging fast-multipole methods as well as boundary elements. Each molecule is coarse-grained as a system of overlapping spheres, whose surface charges are represented by multipole expansions. For details on the method, please see Yap, Head-Gordon (2010) and Yap, Head-Gordon (2013).

Todo

If there's only one mode to PBAM, let's call it `pbsam` instead of `pbsam-auto`.

The current implementation of PB-SAM in APBS includes:

- Calculation of energies, forces and torques
- Calculation of electrostatic potentials
- Brownian dynamics simulations

Keywords for this calculation type include:

exp

This keyword can be used to load in the expansion matrices from files. They will have been previously generated, and will be named `molm.H, F.[s].exp` (see *pbam-auto* for more information). The syntax is:

```
exp {prefix}
```

where `prefix` is the filename prefix `molmsph`. The *H* or *F* and `s.bin` will be appended during the program run.

Todo

It would be better to generalize the *READ input file section* section of the input file rather than use the `exp` command. This command also needs to be cleaned up – it's too fragile. Documented at https://github.com/Electrostatics/apbs-pdb2pqr/issues/489

imat

This keyword can be used to load in the surface integral matrices previously generated by PB-SAM named as `molmsphs.bin` for molecule ID *s* and coarse-grained sphere *s* (see *pbam-auto* for more information). The syntax is:

```
imat {prefix}
```

where `prefix` is the filename prefix `molmsph`. The `s.bin` will be appended during the program run.

Todo

It would be better to generalize the *READ input file section* section of the input file rather than use the `imat` command. This command also needs to be cleaned up – it's too fragile. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/495

msms

Use this flag to call the MSMS program from APBS. MSMS must be installed. Its output, a .vert file is necessary for the coarse-graining process.

Todo

The `msms` keyword should be removed and replaced with a more general alternative: either the *mesh* surface option in *tabi* or the existing APBS *srfm (elec)*. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/497

surf

This keyword can be used to load in the MSMS vertex file for coarse-graining (see *pbsam-auto*) The syntax is:

```
surf {prefix}
```

where `prefix` refers to the filename :file:{prefix}.vert‘.

Todo

The PB-SAM `surf` command is redundant with and should be replaced by the existing *usemesh* command. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/502

tolsp

This is an undocumented parameter from the PB-SAM code that does something with the coarseness of the molecule representation. The PB-SAM authors recommend a value of 2.5.

Todo

We need documentation for `tolsp`. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/504

Background information

PB-SAM is a semi-analytical solution to the linearized Poisson-Boltzmann equation for multiple molecules of arbitrary charge distribution in an ionic solution. The solution is an extension of the analytical method, leveraging Fast-Multipole methods as well as boundary elements. Each molecule is coarse-grained as a system of overlapping spheres, whose surface charges are represented by the multipole expansions $H^{(i)}$ and $F^{(i)}$. To solve for the potential, the following interactions are considered:

- Intra-molecular interactions between overlapping spheres are treated numerically
- Intra-molecular interactions between non-overlapping spheres are treated analytically
- Inter-molecular interactions between spheres on different molecules

With these interactions, the multipole expansions are solved with an iterative SCF method, briefly given as

$$H^{(i,k)} = I_E^{(i,k)} \cdot \left(H^{(i,k)} + F^{(i,k)} + T \cdot H^{(j,l)} \right)$$
$$F^{(i,k)} = I_E^{(i,k)} \cdot \left(H^{(i,k)} + F^{(i,k)} + T \cdot F^{(j,l)} \right)$$

Where $H^{(i)}$ and :math‘F^{(i)}‘ are multipole expansions, $I_E^{(i,k)}$ is the exposed surface integral matrix for sphere k of molecule i, and T is an operator that transforms the multipole expansion to a local coordinate frame.

From the above formulation, computation of the interaction energy $\Omega^{(i)}$ for molecule i, is given as a sum of all the interactions of spheres k within it with all external spheres (in a simplified form) as follows:

$$\Omega^{(i)} = \frac{1}{\epsilon_s} \left\langle \sum_{k\,in\,i} \sum_{j \neq i}^{N} \sum_{l\,in\,j} T \cdot H^{(j,l)}, H^{(i,k)} \right\rangle$$

where $\langle M, N \rangle$ denotes the inner product.

When energy is computed, forces follow as:

$$\mathbf{F}^{(i)} = \nabla_i \Omega^{(i)} = \frac{1}{\epsilon_s} [\langle \nabla_i \, T \cdot H^{(j,l)}, H^{(i,k)} \rangle + \langle T \cdot H^{(j,l)}, \nabla_i \, H^{(i,k)} \rangle$$

The method to calculate the torque is discussed in Yap, Head-Gordon (2013).

PB-SAM files

Vertex/surface file

As part of the coarse-graining process a definition of the molecular surface is necessary. For this we have historically used the program MSMS or on the *online MSMS web server* <http://mgl.scripps.edu/people/sanner/html/msms_server.html>‘_. Within APBS, the user can implement the *msms* flag and the program will be run through APBS, but the executable must be included in your path.

If using the command-line MSMS tool, after downloading it for the correct platform, it can be run as follows:

```
./msms.system -if {filename}.xyzr -of {outfile}
```

It requires an *filename*`.xyzr` file as input, which is the xyz coordinates of each atom of the system followed by the VdW radius. This information can all be found in the PQR file. MSMS will produce *outfile*`.face` and *outfile*`.vert` file. The vertex file is used to coarse-grain the molecule. Once this has been generated, it can be used again as input using the *surf* command.

Coarse-grained PQR file

The coarse-graining process will produce a new PQR file `mol#_cg.pqr` that contains the original PQR concatenated with coarse-graining spherical centers. The number # refers to the order the file was read during the *READ input file section* statements.

IMAT: surface integral file

The surface integrals are computed for the boundary element part of PB-SAM. Their calculation can be quite time-consuming, so the first time they are computed for a system, they are saved to the working directory with the name `mol`*m*`sphs`*s*`.bin`. The *m* in `mol`*m*`sphs`*s*`.bin` is the ordered ID of the molecule from the PQR section. The *s* in `mol`*m*`sphs`*s*`.bin` refers to coarse-grained sphere *s* of the molecule.

Multipole expansion files

Much like the IMAT files, the expansion files are files generated from self-polarization that are useful and time-saving methods for running a system of full-mutual polarziation on many molecules. If no expansion path is provided, the program will calculate self-polarization for each type of molecule in the system and save files of the form `mol`*m*`H,F.`*s*`.exp`, where *m* is the molecule ID, *H* and *F* refer to the respective expansion (see above), and *s* is the coarse-grained sphere number.

APOLAR input file section

This section is the main component for apolar solvation calculations in APBS runs. There may be several APOLAR sections, operating on different molecules or using different parameters for multiple runs on the same molecule. The syntax of this section is:

```
APOLAR [name id]
  <keywords...>
END
```

The first (optional) argument is:

```
name <id>
```

where `id` is a unique string which can be assigned to the calculation to facilitate later operations (particularly in the *PRINT input file section* statements). The `keywords...` describing the parameters of the apolar calculation are discussed in more detail below:

dpos

This is the displacement used for finite-difference-based calculations of surface area derivatives. I know, this is a terrible way to calculate surface area derivatives – we're working on replacing it with an analytic version. In the meantime, please use this parameter with caution. If anyone has code for a better method, please share!

The syntax is:

```
dpos {displacement}
```

where `displacement` is a floating point number indicating the finite difference displacement for force (surface area derivative) calculations in units of Å.

Warning: This parameter is very dependent on `sdens` (see *sdens*); e.g., smaller values of `dpos` require larger values of `sdens`.

gamma

This keyword specifies the surface tension coefficient for apolar solvation models.

```
gamma { value }
```

where `value` is a floating point number designating the surface tension in units of kJ mol^{-1} $Å^{-2}$. This term can be set to zero to eliminate the SASA contributions to the apolar solvation calculations.

Todo

Resolve unit confusion with geometric flow *gamma* keyword. https://github.com/Electrostatics/apbs-pdb2pqr/issues/490

press

This term specifies the solvent pressure in kJ mol^{-1} $Å^{-3}$. This coefficient multiplies the volume term of the apolar model and can be set to zero to eliminate volume contributions to the apolar solvation calculation. The syntax is:

```
press {value}
```

where `value` is the floating point value of the pressure coefficient in kJ mol^{-1} $Å^{-3}$.

Todo

Resolve unit confusion with geometric flow `press` keyword and the apolar *press* keyword. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/499

srfm (apolar)

This keyword specifies the model used to construct the solvent-related surface and volume. The syntax is:

```
srfm {flag}
```

where `flag` is a string that specifies the model used for surface and volume. Acceptable values of flag include:

sacc Solvent-accessible (also called "probe-inflated") surface and volume.

APBS apolar calculations follow the very generic framework described in Wagoner JA, Baker NA. Assessing implicit models for nonpolar mean solvation forces: the importance of dispersion and volume terms. Proc Natl Acad Sci USA, 103, 8331-8336, 2006. doi:10.1073/pnas.0600118103. ' Nonpolar solvation potentials of mean force (energies) are calculated according to:

$$W^{(\mathrm{np})}(x) = \gamma A(x) + pV(x) + \bar{\rho}\sum_{i=1}^{N}\int_{\Omega} u_i^{(\mathrm{att})}(x_i, y)\theta(x, y)\,\mathrm{d}y$$

and mean nonpolar solvation forces are calculated according to:

$$\mathbf{F}_i^{(\mathrm{np})}(x) = -\gamma\frac{\partial A(x)}{\partial x_i} - p\int_{\Gamma_i(x)}\frac{y - x_i}{\|y - x_i\|}\,\mathrm{d}y - \bar{\rho}\sum_{i=1}^{N}\int_{\Omega}\frac{\partial u_i^{(\mathrm{att})}(x_i, y)}{\partial x_i}\theta(x, y)\,\mathrm{d}y$$

In these equations, γ is the repulsive (hard sphere) solvent surface tension (see *gamma*), A is the conformation-dependent solute surface area (see *srad* and *srfm (apolar)* keywords), p is the repulsive (hard sphere) solvent pressure (see *press* keyword), V is the conformation-dependent solute volume (see *srad* and *srfm (apolar)* keywords), ρ (see *bconc* keywords) is the bulk solvent density, and the integral involves the attractive portion (defined in a Weeks-Chandler-Andersen sense) of the Lennard-Jones interactions between the solute and the solvent integrated over the region of the problem domain outside the solute volume V. Lennard-Jones parameters are taken from APBS parameter files as read in through an APBS input file READ statement (see *READ input file section*).

Note: The above expressions can easily be reduced to simpler apolar solvation formalisms by setting one or more of the coefficients to zero through the keywords.

Warning: All APOLAR calculations require a parameter file which contains Lennard-Jones radius and well-depth parameters for all the atoms in the solute PDB. This parameter file must also contain radius and well-depth parameters for water (specifically: residue "WAT" and atom "OW"). Complete parameter files for protein and nucleic acid parameters are not currently available; we prefer geometric flow calculations (coupled polar and apolar components) rather than this model.

PRINT input file section

This is a very simple section that allows linear combinations of calculated properties to be written to standard output. The syntax of this section is:

```
PRINT {what} [id op id op...] END
```

The first mandatory argument is `what`, the quantity to manipulate or print. This variable is a string that can assume the following values:

elecEnergy Print electrostatic energies as calculated with an earlier *ELEC input file section calcenergy* command.

elecForce Print electrostatic forces as calculated with an earlier *ELEC input file section calcforce* command.

apolEnergy Print apolar energies as calculated with an earlier *APOLAR input file section calcenergy* command.

apolForce Print electrostatic forces as calculated with an earlier *APOLAR input file section calcforce* command.

The next arguments are a series of `id op id op id op ... id` commands where every `id` is immediately followed by an `op` and another `id`.

id This is a variable string or integer denoting the ID of a particular *ELEC input file section* or *APOLAR input file section* calculations. String values of `id` correspond to the optional "names" that can be assigned to *ELEC input file section* or *APOLAR input file section* calculations. Integer values of id are assumed to corresponding to the sequentially-assigned integer IDs for *ELEC input file section* or *APOLAR input file section* calculations. These IDs start at 1 and are incremented (independently) for each new *ELEC input file section* or *APOLAR input file section* calculation.

op Specify the arithmetic operation (+ for addition and − for subtraction) to be performed on the calculated quantities

For example:

```
# Energy change due to binding
print energy complex - ligand - protein end
# Energy change due to solvation
print energy solvated - reference end
# Solvation energy change due to binding
print energy complex_solv - complex_ref - ligand_solv + ligand_ref - protein_solv +␣
↪protein_ref end
```

Solvation model background

Solvation Models

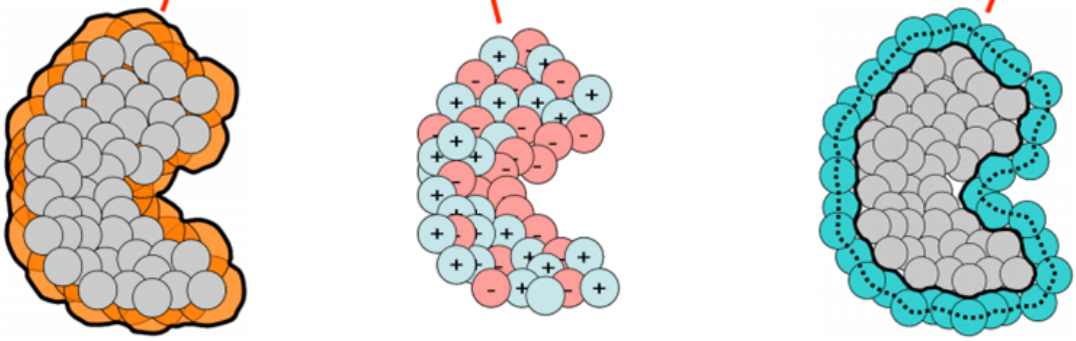
Electrostatic and solvation models can be roughly divided into two classes (*[Warshel2006]*, *[Roux1999]*, *[Ren2012]*) explicit solvent models that treat the solvent in atomic detail and implicit solvent models that generally replace the explicit solvent with a dielectric continuum. Each method has its strengths and weaknesses. While explicit solvent models offer some of the highest levels of detail, they generally require extensive sampling to converge properties of interest. On the other hand, implicit solvent models trade detail and some accuracy for the "pre-equilibration" of solvent degrees of freedom and elimination of sampling for these degrees of freedom. Implicit solvent methods are popular for a variety of biomedical research problems.

The polar solvation energy is generally associated with a difference in charging free energies in vacuum and solvent. A variety of implicit solvent models are available to biomedical researchers to describe polar solvation; however, the most widely-used methods are currently the Generalized Born (GB) and Poisson-Boltzmann (PB) models. GB and related methods are very fast heuristic models for estimating the polar solvation energies of biomolecular structures and therefore are often used in high-throughput applications such as molecular dynamics simulations. PB methods can be formally derived from more detailed theories and offer a somewhat slower, but often more accurate, method for evaluating polar solvation properties and often serve as the basis for parameterization and testing of GB methods. Finally, unlike most GB methods, PB models provide a global solution for the electrostatic potential and field within and around a biomolecule, therefore making them uniquely suited to visualization and other structural analyses, diffusion simulations, and a number of other methods which require global electrostatic properties.

The PB equation (*[Fogolari2002]*, *[Lamm2003]*, *[Grochowski2007]*, *[Baker2005]*) is a nonlinear elliptic partial differential equation of the form shown in the figure below which is solved for the electrostatic potential. The coefficients of this equation are directly related to the molecular structure of the system under consideration. PB theory is approximate and, as a result, has several well-known limitations which can affect its accuracy (*[Grochowski2007]*, *[Netz2000]*), particularly for strongly charged systems or high salt concentrations. However, despite these limitations, PB methods are still very important for biomolecular structural analysis, modeling, and simulation. Furthermore, these limitations are currently being addressed through new implicit solvent models and hybrid treatments which extend the

applicability of PB theory while preserving some of its computational efficiency. There are currently examples of both types of treatments which leverage APBS ([Azuara2006], [Chu2007], [Vitalis2004]).

$$-\nabla \cdot \epsilon(\mathbf{x})\nabla\phi(\mathbf{x}) = \rho_f(\mathbf{x}) + \sum_m q_m c_m e^{-\beta[q_m\phi(\mathbf{x})+V_m(\mathbf{x})]}$$



$$G[\phi] = \frac{1}{4\pi}\int_\Omega \left\{ \rho_f(\mathbf{x})\phi(\mathbf{x}) - \frac{\epsilon(\mathbf{x})}{2}[\nabla\phi(\mathbf{x})]^2 + \sum_m c_m e^{-\beta V_m(\mathbf{x})}\left[e^{-\beta q_m\phi(\mathbf{x})} - 1\right] \right\} d\mathbf{x}$$

$$\mathbf{F}_i[\phi] = -\frac{\partial G[\phi]}{\partial \mathbf{r}_i} = -\frac{1}{4\pi}\int_\Omega \left\{ \frac{\partial \rho_f(\mathbf{x})}{\partial \mathbf{r}_i}\phi(\mathbf{x}) - \frac{1}{2}\frac{\partial \epsilon(\mathbf{x})}{\partial \mathbf{r}_i}[\nabla\phi(\mathbf{x})]^2 + \sum_m c_m \frac{\partial e^{-\beta V_m(\mathbf{x})}}{\partial \mathbf{r}_i}\left[e^{-\beta q_m\phi(\mathbf{x})} - 1\right] \right\} d\mathbf{x}$$

Reaction field

Dielectric boundary

"Osmotic"

PB methods provide polar solvation energies and therefore must be complemented by non-polar solvation models to provide a complete view of biomolecular solvent-solute interactions. non-polar solvation is generally associated with the insertion of the uncharged solute into solvent. There are many non-polar solvation models available; however, work by Levy et al. [Levy2003] as well as our own research [Wagoner2006] has demonstrated the importance of non-polar implicit solvent models which include treatment of attractive solute-solvent dispersion terms. This model has been implemented in APBS and can also be easily transformed into simpler popular non-polar models (e.g., solvent-accessible surface area). While this model can be used separately from PB to analyze non-polar contributions to solvation energy, its preferred use is coupled to the PB equation through a geometric flow model [Chen2010] which treats polar and non-polar interactions in the same framework and reduces the number of user-specified empirical parameters.

Further Reading

Caveats and sources of error

Model error

When performing solvation calculations using APBS, it is important to keep in mind that you are using an approximate model for solvation. Therefore, your answers may contain errors related to approximations in the model. Many review articles have covered the nature of these approximations, we will stress the highlights below.</p>

Linear dielectric response

The Poisson-Boltzmann equation models the solvent as a dielectric continuum that responds linearly to all applied fields. In particular, under this model, very strong fields can induce unrealistically strong polarization in the dielectric media representing the solvent and/or the solute interior. However, molecular solvents or solutes cannot support an infinite amount of polarization: they are limited by their density, their finite dipole moments, and their finite degree of electronic polarizability. Therefore, the continuum model assumption of linear dielectric response can break down in situations with strong electric fields; e.g., around nucleic acids or very highly-charged proteins.

Local dielectric response

The Poisson-Boltzmann equation models the solvent as a dielectric continuum that also responds locally to all applied fields. n other words, under this model, the local polarization at a point x is only dependent on the field at point x. However, molecular solvents and solutes clearly don't obey this assumption: the variety of covalent, steric, and other non-bonded intra- and inter-molecular interactions ensures that the polarization at point x is dependent on solute-field interactions in a non-vanishing neighborhood around x. One way to limit the impact of this flawed assumption, is to model solute response as "explicitly" as possible in your continuum electrostatics problems. In other words, rather than relying upon the continuum model to reproduce conformational relaxation or response in your solute, model such response in detail through molecular simulations or other conformational sampling.

Ambiguity of dielectric interfaces and coefficient values

Violation of the assumptions of linear and local dielectric response in real molecular systems leads to serious ambiguity in the definition of the dielectric coefficient in the Poisson-Boltzmann equation. In particular, while the values for bulk solvent (i.e., far away from the solute) response are well-defined, all other values of the dielectric coefficient are ambiguous. In general, continuum models assume a constant low-dielectric value inside the solute and the bulk solvent value outside the solute. This assumption creates tremendous sensitivity of calculation results on the placement of the dielectric interface (usually determined by solute atomic radii) and the specific value of the internal solute dielectric. In general, errors arising from this assumption can be minimized by using internal dielectric values that are consistent with the solute atomic radii parameterization.

No specific ion-solvent or ion-solute interactions

Most Poisson-Boltzmann models assume that ions do not interact directly with the solvent: they are charges embedded in the same dielectric material as the bulk solvent. This assumption implies that ions experience no "desolvation" penalty as they interact with the solute surface. Additionally, most Poisson-Boltzmann models assume that ions interaction with the solute only through electrostatic and hard-sphere steric potentials. However, this assumption neglects some of the subtlety of ion-protein interactions; in particular, dispersive interactions that can possibly lead to some degree of ion specificity.

Mean field ion behavior

Finally, the Poisson-Boltzmann model is a "mean field" description of ionic solutions. This means that ions only experience the average influence of other ions in the system; the model neglects fluctuations in the ionic atmosphere and correlations between the ions in solution. Such correlations and fluctuations can be very important at high ionic charge densities; e.g., for multivalent ions, high ion concentrations, or the high-density ionic regions near highly-charged biomolecules.

Parameter set errors

Todo

Under construction; please see https://arxiv.org/abs/1705.10035 for an initial discussion. Saved as issue https://github.com/Electrostatics/apbs-pdb2pqr/issues/481

Structure-based errors

Electrostatics calculations can be very sensitive to errors in the structure, including:

- Misplaced atoms or sidechains
- Missing regions of biomolecular structure
- Incorrect titration state assignments

Of these errors, incorrect titration states are the most common and, often, the most problematic. The software package PDB2PQR was created to minimize all of the above problems and we recommend its use to "pre-process" structures before electrostatics calculations.

Discretization error

The Poisson-Boltzmann partial differential equation must be discretized in order to be solved on a computer. APBS discretizes the equation in spacing by evaluating the problem coefficients and solving for the electrostatic potential on a set of grid (finite difference) or mesh (finite element) points. However, this discretization is an approximation to the actual, continuously-specified problem coefficients. Coarser discretization of coefficients and the solution reduce the overall accuracy and introduce errors into the final potential and calculated energies.

It is very important to evaluate the sensitivity of your calculated energies to the grid spacings and lengths. In general, it is a good idea to scan a range of grid spacings and lengths before starting a problem and choose the largest problem domain with the smallest grid spacing that gives consistent results (e.g., results that don't change as you further reduce the grid spacing).

Solver and round-off error

APBS uses iterative solvers to solve the nonlinear algebraic equations resulting from the discretized Poisson-Boltzmann equation. Iterative solvers obtain solutions to algebraic equations which are accurate within a specified error tolerance. Current versions of APBS use a fixed error tolerance of 10^{-6} which implies approximately 1 part per million root-mean-squared error in calculated potentials. Such error tolerances have been empirically observed to give good accuracy in the calculated energies obtained with APBS.

However, it is important to note that the error in potential does not necessarily directly relate to the error in the energies calculated by APBS. In particular, most meaningful energies are calculated as differences between energies from several calculations. While the accuracy of each separate energy can be related to the solver error tolerance, the energy difference can only be loosely bounded by the error tolerance.

This issue is illustrated in the protein kinase ligand binding example provided with APBS as `pka-lig` and analyzed below. This example demonstrates that, while the errors for each calculation remain small, the overall error in the computed energy can be very large; particularly when two different methods are compared.

Table 6.2: Sensitivity of PB energies to iterative solver error tolerance (APBS 1.2)

Error tolerance	Protein energy	Protein energy relative error (with respect to 10^{-12} tolerance)	Ligand energy	Ligand energy relative error (with respect to 10^{-12} tolerance)	Complex energy	Complex energy relative error (with respect to 10^{-12} tolerance)	Binding energy	Binding energy relative error (with respect to 10^{-12} tolerance)
1.00E-06	3.01E+03	1.47E-08	1.05E+04	1.42E-08	3.11E+02	1.45E-08	8.08E+00	7.75E-06
1.00E-09	3.01E+03	1.19E-11	1.05E+04	1.71E-11	3.11E+02	1.45E-08	8.08E+00	2.48E-09
1.00E-12	3.01E+03	1.00E+00	1.05E+04	1.00E+00	3.11E+02	1.00E+00	8.08E+00	1.00E+00

APBS utilities

APBS is distributed with utilities designed to simplify typical tasks associated with electrostatics calculations.

amber2charmm.sh

A bash script for converting AMBER atom names to CHARMM names. Found in `tools/conversion`

del2dx

Converts DelPhi-format map files (electrostatic potential, etc.) to APBS OpenDX format. Found in `tools/mesh`

dx2mol

Converts OpenDX format map files to MolMol format. Found in `tools/mesh`

dx2uhbd

Converts OpenDX format map files to UHBD format. Found in `tools/mesh`

qcd2pqr.awk

An awk script for converting from UHBD QCD format to PQR format.

uhbd_asc2bin

Converts UHBD ASCII-format files to binary format. Found in `tools/mesh`

WHATIF2AMBER.sed

A sed script for converting WHATIF atoms names to the AMBER naming scheme. Found in `tools/conversion`

benchmark

Benchmark file I/O for reading/writing scalar data. Found in `tools/mesh`

analysis

Calculates various metrics from input scalar data. Found in `tools/mesh`

born

Calculate generalized Born forces and energies. Found in `tools/manip`

coulomb

Calculate Coulomb forces and energies. Found in `tools/manip`

dxmath

Performs simple arithmetic operations with Cartesian grid data. This program takes as input a file with operations specified in a stack-based (RPN) manner. For example, a command file which adds grid1 and grid2, multiplies the result by 5.3, adds grid4, subtracts 99.3 from the whole thing, and writes the result on grid5 would have the form:

```
grid1
grid2 +
5.3 *
grid4 +
99.3 -
grid5 =
```

The file names, scalar values, and operations must be separated by tabs, line breaks, or white space. Comments can be included between the character # and a new line (in the usual shell script fashion). Found in `tools/mesh`

inputgen.py

Create an APBS input file using *psize.py* data. Found in `tools/manip`

mergedx and mergedx2

Combine multiple OpenDX files into a single resampled file. mergedx2 can perform a number of grid manipulation operations, including:

- Combining multiple OpenDX map files
- Resampling of one or more OpenDX map files (for example to alter the grid spacing of separate OpenDX files for further manipulation)
- Extracting a subregion of an existing OpenDX map file.

Found in `tools/mesh`

mgmesh

Prints out acceptable combinations of *nlev* and *dime* for multigrd calculations. Found in `tools/mesh`

multivalue

This program evaluates OpenDX scalar data at a series of user-specified points and returns the value of the data at each point. Found in `tools/mesh`

psize.py

Suggest grid sizes and spacings for APBS given an input molecule. Found in `tools/manip`

similarity

Computes similarity between two scalar grid datasets. Found in `tools/mesh`

smooth

Convolve grid data with various filters. Found in `tools/mesh`

APBS programmer's guide

The APBS programmer's guide is generated by Doxygen and available for download as a `ZIP file`.

Todo

Move Programmer's Guide to Sphinx.

APBS license

Nathan A. Baker (nathanandrewbaker@gmail.com), Pacific Northwest National Laboratory

Additional contributing authors listed in the code documentation.

- Neither the name of the developer nor the names of its contributors may be used to endorse or promote products derived from this software without specific prior written permission.

CHAPTER 7

Other software

This page provides links to other software packages which are commonly used with APBS-PDB2PQR.

Calculation setup and visualization

See *Visualizing results*.

Dynamics simulations

The iAPBS library was developed to facilitate the integration of APBS with other molecular simulation packages. This library has enabled the integration of APBS with several molecular dynamics packages, including NAMD, AMBER, and CHARMM.

APBS is also used directly by Brownian dynamics software such as SDA and BrownDye.

CHAPTER 8

File formats

Mesh and scalar data formats

OpenDX scalar data format

We output most discretized scalar data (e.g., potential, accessibility, etc.) from APBS in the data format used by the OpenDX software package. The OpenDX data format is very flexible; the following sections describe the application of this format for APBS multigrid and finite element datasets.

The multigrid data format has the following form:

```
object 1 class gridpositions counts nx ny nz
origin xmin ymin zmin
delta hx 0.0 0.0
delta 0.0 hy 0.0
delta 0.0 0.0 hz
object 2 class gridconnections counts nx ny nz
object 3 class array type double rank 0 items n data follows
u(0,0,0) u(0,0,1) u(0,0,2)
...
u(0,0,nz-3) u(0,0,nz-2) u(0,0,nz-1)
u(0,1,0) u(0,1,1) u(0,1,2)
...
u(0,1,nz-3) u(0,1,nz-2) u(0,1,nz-1)
...
u(0,ny-1,nz-3) u(0,ny-1,nz-2) u(0,ny-1,nz-1)
u(1,0,0) u(1,0,1) u(1,0,2)
...
attribute "dep" string "positions"
object "regular positions regular connections" class field
component "positions" value 1
component "connections" value 2
component "data" value 3`
```

The variables in this format include:

nx ny nz The number of grid points in the x-, y-, and z-directions

xmin ymin zmin The coordinates of the grid lower corner

hx hy hz The grid spacings in the x-, y-, and z-directions.

n The total number of grid points; $n = nx * ny * nz$

u(*,*,*) The data values, ordered with the z-index increasing most quickly, followed by the y-index, and then the x-index.

For finite element solutions, the OpenDX format takes the following form:

```
object 1 class array type float rank 1 shape 3 items N
v1x v1y v1z
v2x v2y v2z
...
vNx vNy vNz
object 2 class array type int rank 1 shape 4 items M
s1a s1b s1c s1d
s2a s2b s2c s2d
...
sMa sMb sMc sMd
attribute "element type" string "tetrahedra"
object 3 class array type float rank 0 items N
u1
u2
...
uN
attribute "dep" string "positions"
object "irregular positions irregular connections" class field
component "positions" value 1
component "connections" value 2
component "data" value 3
end
```

where the variables in this format are:

N Number of vertices

vix viy viz Coordinates of vertex i

M Number of simplices

sia sib sic sid IDs of vertices in simplex i

ui Data value associated with vertex i

MCSF mesh format

APBS reads and writes meshes in the *FEtk MCSF format <http://fetk.org/codes/mc/>*.

UHBD scalar data format

We also support scalar data output in the legacy "UHBD format" for use with programs such as UHBD and SDA.

UHBD data is written in the format:

```
/* Write out the header */
Vio_printf(sock, "%72s\n", title);
Vio_printf(sock, "%12.5e%12.5e%7d%7d%7d%7d%7d\n", 1.0, 0.0, -1, 0,
  nz, 1, nz);
Vio_printf(sock, "%7d%7d%7d%12.5e%12.5e%12.5e%12.5e\n", nx, ny, nz,
  hx, (xmin-hx), (ymin-hx), (zmin-hx));
Vio_printf(sock, "%12.5e%12.5e%12.5e%12.5e\n", 0.0, 0.0, 0.0, 0.0);
Vio_printf(sock, "%12.5e%12.5e%7d%7d", 0.0, 0.0, 0, 0);

/* Write out the entries */
icol = 0;
for (k=0; k<nz; k++) {
    Vio_printf(sock, "\n%7d%7d%7d\n", k+1, thee->nx, thee->ny);
    icol = 0;
    for (j=0; j<ny; j++) {
        for (i=0; i<nx; i++) {
            u = k*(nx)*(ny)+j*(nx)+i;
            icol++;
            Vio_printf(sock, " %12.5e", thee->data[u]);
            if (icol == 6) {
                icol = 0;
                Vio_printf(sock, "\n");
            }
        }
    }
}
```

Molecular structure formats

PQR molecular structure format

This format is a modification of the PDB format which allows users to add charge and radius parameters to existing PDB data while keeping it in a format amenable to visualization with standard molecular graphics programs. The origins of the PQR format are somewhat uncertain, but has been used by several computational biology software programs, including MEAD and AutoDock. UHBD uses a very similar format called QCD.

APBS reads very loosely-formatted PQR files: all fields are whitespace-delimited rather than the strict column formatting mandated by the PDB format. This more liberal formatting allows coordinates which are larger/smaller than $\pm$ 999 Å. APBS reads data on a per-line basis from PQR files using the following format::

```
Field_name Atom_number Atom_name Residue_name Chain_ID Residue_number X Y Z Charge␣
↪Radius
```

where the whitespace is the most important feature of this format. The fields are:

Field_name A string which specifies the type of PQR entry and should either be ATOM or HETATM in order to be parsed by APBS.

Atom_number An integer which provides the atom index.

Atom_name A string which provides the atom name.

Residue_name A string which provides the residue name.

Chain_ID An optional string which provides the chain ID of the atom. Note that chain ID support is a new feature of APBS 0.5.0 and later versions.

Residue_number An integer which provides the residue index.

X Y Z 3 floats which provide the atomic coordinates (in Å)

Charge A float which provides the atomic charge (in electrons).

Radius A float which provides the atomic radius (in Å).

Clearly, this format can deviate wildly from PDB due to the use of whitespaces rather than specific column widths and alignments. This deviation can be particularly significant when large coordinate values are used. However, in order to maintain compatibility with most molecular graphics programs, the PDB2PQR program and the utilities provided with APBS attempt to preserve the PDB format as much as possible.

PDB molecular structure format

The PDB file format is described in detail in the Protein Data Bank documentation.

MOL2 molecular structure format

The MOL2 file format is a popular method for specifying chemical structure, including atom types, positions, and bonding. It is described in detail in the Tripos documentation.

XML molecular structure format

The XML structure format was designed as a light-weight alternative to remediate some of the shortcomings of the flat-file format. By use of XML, issues related to extra fields in the file or columns merging together can easily be remedied. Additionally, APBS will only parse the necessary information from the XML file and will ignore all other information, so users wishing to store extra data related to a residue or atom can do so inline without affecting APBS.

This data format has the following form:

```
<roottag>
   <residue>
       <atom>
           <x>x</x>
           <y>y</y>
           <z>z</z>
           <charge>charge</charge>
           <radius>radius</radius>
       </atom>
       ...
   </residue>
   ...
</roottag>
```

The variables in this example are:

roottag This is the root element of the XML file. The value is not important to APBS - APBS simply checks that it is closed at the end of the file.

x y z A float giving the {x, y, z}-coordinate of the atom in Å.

charge A float giving the atomic charge (in electrons).

atomradius A float giving the atomic Radius (in Å).

Note: Yes, we probably should have used PDBML instead.

Matrix formats

Harwell-Boeing matrix format

This is the sparse matrix output format used by APBS for analyses of the matrix operators which are constructed during PB solution. This format was implemented so matrix operators could by decomposed with SuperLU and ARPACK but this also serves as a useful general mechanism for sparse matrix input and output.

Parameter formats

APBS XML parameter format

This parameter file format has the following form:

```
<ffname>
   <residue>
       <name>resname</name>
       <atom>
           <name>atomname</name>
           <charge>atomcharge</charge>
           <radius>atomradius</radius>
           <epsilon>atomepsilon</epsilon>
       </atom>
       ...
   </residue>
   ...
</ffname>
```

The variables in this example are:

ffname The name of the forcefield. This is the root element of the XML file.

resname A string giving the residue name, as provided in the PDB file to be parameterized.

atomname A string giving the atom name, as provided in the PDB file to be parameterized.

atomcharge A float giving the atomic charge (in electrons).

atomradius A float giving the atomic Radius (in Å).

atomepsilon A float giving the Lennard-Jones well depth ϵ (in kJ/mol). This is used for the calculation of WCA energies in apolar solvation energies and forces. We assume that the Lennard-Jones potential is defined in the "AMBER style"

PDB2PQR NAMES files

Much of the difficulty in adding a new forcefield to PDB2PQR depends on the naming scheme used in that forcefield.

XML file format

To start, either a flat file or XML file containing the desired forcefield's parameters should be made - see `AMBER.DAT` and `AMBER.xml` for examples. If the forcefield's naming scheme matches the canonical naming scheme, that's all that is necessary. If the naming schemes differ, however, conversions must be made. These are made in the `*.names` file (see `CHARMM.names`, for example). In this file you will see sections like:</p>

```
<residue>
  <name>WAT</name>
  <useresname>TP3M</useresname>
  <atom>
    <name>O</name>
    <useatomname>OH2</useatomname>
  </atom>
</residue>
```

This section tells PDB2PQR that for the oxygen atom O in WAT, CHARMM uses the names OH2 and TP3M, respectively. When the XML file is read in, PDB2PQR ensures that the WAT/O pair points to TP3M/OH2 such that the appropriate parameters are returned. But for naming schemes that greatly differ from the PDB2PQR canonical naming scheme, this could get really ugly. As a result, PDB2PQR can use regular expressions to simplify the renaming process, i.e.:

```
<residue>
  <name>[NC]?...$</name>
  <atom>
    <name>H</name>
    <useatomname>HN</useatomname>
  </atom>
</residue>
```

This section of code will ensure that the H atom of all canonical residue names that match the `[NC]?...$` regular expression point to HN instead. This regular expression matches all three-letter residue names, residue names with an 'N' prepended (N-Termini), and residue names with a 'C' prepended (C-Termini). For twenty amino acids, sixty residue name changes can all be done by a single section. The use of regular expressions is therefore a much more powerful method of handling naming scheme differences than working on a one to one basis.

There are a few other additional notes when using the `.names` file. First, the `$group` variable is used to denote the matching group of a regular expression, for instance:

```
<residue>
  <name>HI([PDE])$</name>
  <useresname>HS$group</useresname>
</residue>
```

This section replaces HIP/HID/HIE with HSP/HSD/HSE by first matching the HI([PDE])$ regular expression and then using the group that is enclosed by parantheses to fill in the name to use.

Second, sections are cumulative - since CHARMM, for instance, has a patch-based naming scheme, one single canonical residue name can map to multiple forcefield-scheme names. Let's look at how to map an SS-bonded Cysteine (canonical name CYX) to the CHARMM naming scheme:

```
<residue>
  <name>CYX</name>
  <useresname>CYS</useresname>
</residue>
<residue>
  <name>CYX</name>
```

```
  <useresname>DISU</useresname>
  <atom>
    <name>CB</name>
    <useatomname>1CB</useatomname>
  </atom>
  <atom>
    <name>SG</name>
    <useatomname>1SG</useatomname>
  </atom>
</residue>
```

The CYX residue is first mapped to CHARMM's CYS, and then to CHARMM's DISU object. All atom names that are found in DISU overwrite those found in CYS - in effect, the DISU patch is applied to CYS, yielding the desired CYX. This cumulative can be repeated as necessary.

Caveats about atom naming

In an ideal world each individual residue and atom would have a standard, distinct name. Unfortunately several naming schemes for atoms exist, particularly for hydrogens. As such, in order to detect the presence/absence of atoms in a protein, an internal canonical naming scheme is used. The naming scheme used in PDB2PQR is the one recommended by the PDB itself, and derives from the IUPAC naming recommendations[1]

This canonical naming scheme is used as the default PDB2PQR output. All conversions in PDB2PQR use the internal canonical naming scheme to determine distinct atom names. In previous versions of PDB2PQR, these conversions were stored in long lists of if statements, but for transparency and editing this is a bad thing. Instead, all conversions can now be found in XML as described above.

There are a few additions to the canonical naming scheme, mirrored after the AMBER naming scheme (chosen since for the most part it follows the IUPAC recommendations). These changes are made in `PATCHES.xml`, and allow any of the following to be patched as necessary as well as detected on input:

N* N-Terminal Residue (i.e. NALA, NLEU)

NEUTRAL-N* Neutral N-Terminal Residue

C* C-Terminal Residue (i.e. CLYS, CTYR)

NEUTRAL-C* Neutral C-Terminal Residue

***5** 5-Terminus for Nucleic Acids (i.e. DA5)

***3** 3-Terminus for Nucleic Acids (i.e. DA3)

ASH Neutral ASP

CYX SS-bonded CYS

CYM Negative CYS

GLH Neutral GLU

HIP Positive HIS

HID Neutral HIS, proton HD1 present

HIE Neutral HIS, proton HE2 present

[1] 10. (a) Markley, et al., "Recommendations for the Presentation of NMR Structures of Proteins and Nucleic Acids," Pure & Appl. Chem., 70 (1998): 117-142. DOI:10.1046/j.1432-1327.1998.2560001.x

LYN Neutral LYS

TYM Negative TYR

APBS flat-file parameter format

This parameter file format is a series of lines of the form:

```
Residue_name Atom_name Charge Radius Epsilon
```

where the whitespaces are important and denote separation between the fields. The fields here are:

Residue_name A string giving the residue name, as provided in the PDB file to be parametrized.

Atom_name A string giving the atom name, as provided in the PDB file to be parametrized.

Charge A float giving the atomic charge (in electrons).

Radius A float giving the atomic radius (in Å).

Epsilon A float giving the Lennard-Jones well depth (epsilon, in kJ/mol). This is used for the calculation of WCA energies in apolar solvation energies and forces. We assume that the Lennard-Jones potential is defined in the "AMBER style"

Todo

Migrate PDB2PQR XML format information over from programmer's guide.

CHAPTER 9

APBS-PDB2PQR examples and tutorials

PDB2PQR operations

In order to perform electrostatics calculations on your biomolecular structure of interest, you need to provide atomic charge and radius information to APBS. Charges are used to form the biomolecular charge distribution for the Poisson-Boltzmann (PB) equation while the radii are used to construct the dielectric and ionic accessibility functions.

The PDB2PQR web service and software will convert most PDB files into PQR format with some caveats. Although PDB2PQR can fix some missing heavy atoms in sidechains, it does not currently have the (nontrivial) capability to model in large regions of missing backbone and sidechain coordinates. Be patient and make certain that the job you submitted to the PDB2PQR website has finished and you have downloaded the resulting PQR file correctly. It usually takes less than 10 minutes for the job to finish.

This tutorial assumes that you have registered and have access to the PDB2PQR web server.

Adding hydrogens and assigning parameters

Pick a structure

Start by choosing a PDB file to process. Either enter the 4-character PDB ID into PDB2PQR or accession number (1FAS is a good starting choice) or upload your own PDB file. Note that, if you choose to enter a 4-character PDB ID, PDB2PQR will process all recognizable chains of PDB file as it was deposited in the PDB (e.g., not the biological unit, any related transformations, etc.).

Pick a forcefield

For most applications, the choice is easy: PARSE. This forcefield has been optimized for implicit solvent calculation and is probably the best choice for visualization of protein electrostatics and many common types of energetic calculations for proteins. However, AMBER and CHARMM may be more appropriate if you are attempting to compare directly to simulations performed with those force fields, require nucleic acid support, are simulating ligands parameterized with those force fields, etc.

It is also possible to upload a user-defined forcefield (e.g., to define radii and charges for ligands or unusual residues). Please see *Extending PDB2PQR* for more information.

Pick a naming scheme

This choice is largely irrelevant to electrostatics calculations but may be important for some visualization programs. When in doubt, choose the "Internal naming scheme" which attempts to conform to IUPAC standards.

Reconstruct missing atoms (hydrogens)

Under options, be sure the "Ensure that new atoms are not rebuilt too close to existing atoms" and "Optimize the hydrogen bonding network" options are selected. You can select other options as well, if interested.

Download and view the results

Download the resulting PQR file and visualize in a molecular graphics program to examine how the hydrogens were added and how hydrogen bonds were optimized.

Parameterizing ligands

This section outlines the parameterization of ligands using the PEOE_PB methods (see Czodrowski et al, 2006 for more information).

The PDB structure 1HPX includes HIV-1 protease complexed with an inhibitor at 2.0 Å resolution. HIV-1 protease has two chains; residue D25 is anionic on one chain and neutral on the other – these titration states are important in the role of D25 as an acid in the catalytic mechanism.

Ignoring the ligand

If we don't want to include the ligand, then the process is straightforward:

1. From the PDB2PQR server web page, enter 1HPX into the PDB ID field.
2. Choose whichever forcefield and naming schemes you prefer.
3. Under options, be sure the "Ensure that new atoms are not rebuilt too close to existing atoms", "Optimize the hydrogen bonding network", and "Use PROPKA to assign protonation states at pH" options are selected. Choose pH 7 for your initial calculations. You can select other options as well, if interested.
4. Hit the "Submit" button.
5. Once the calculations are complete, you should see a web page with a link to the PROPKA output, a new PQR file, and warnings about the ligand KNI (since we didn't choose to parameterize it in this calculation). For comparison, you might download the the original PDB file and compare the PDB2PQR-generated structure with the original to see where hydrogens were placed.

Parameterizing the ligand

This section outlines the parameterization of ligands using the PEOE_PB methods (see DOI:10.1002/prot.21110).

Ligand parameterization currently requires a *MOL2-format* representation of the ligand to provide the necessary bonding information. MOL2-format files can be obtained through the PRODRG web server or some molecular modeling

software packages. PRODRG provides documentation as well as several examples on ligand preparation on its web page.

We're now ready to look at the 1HPV crystal structure from above and parameterize its ligand, KNI-272.

1. From the PDB2PQR server web page, enter `1HPX` into the PDB ID field.
2. Choose whichever forcefield and naming schemes you prefer.
3. Under options, be sure the "Ensure that new atoms are not rebuilt too close to existing atoms", "Optimize the hydrogen bonding network", and "Assign charges to the ligand specified in a MOL2 file" options are selected (download the `ligand MOL2 file`). You can select other options as well, if interested.
4. Hit the "Submit" button.
5. Once the calculations are complete, you should see a web page with a link to the new PQR file with a warning about debumping P81 (but no warnings about ligand parameterization!).

As a second example, we use the PDB structure 1ABF of L-arabinose binding protein in complex with a sugar ligand at 1.90 Å resolution. To parameterize both this protein and its ligand:

1. From the PDB2PQR server web page, enter *1ABF* into the PDB ID field.
2. Choose whichever forcefield and naming schemes you prefer.
3. Under options, be sure the "Ensure that new atoms are not rebuilt too close to existing atoms", "Optimize the hydrogen bonding network", and "Assign charges to the ligand specified in a MOL2 file" options are selected (download the `ligand MOL2 file`). You can select other options as well, if interested.
4. Hit the "Submit" button.
5. Once the calculations are complete, you should see a web page with a link to the new PQR file with a warning about debumping P66, K295, and K306 (but no warnings about ligand parameterization!).

APBS examples

APBS examples start with a PQR file (e.g., generated by PDB2PQR). Some of these examples can be performed through the PDB2PQR web interface but most require a command-line APBS program.

Solvation energies with APBS

Solvation energies are usually decomposed into a free energy cycle as shown in the free energy cycle below. Note that such solvation energies often performed on fixed conformations; as such, they are more correctly called "potentials of mean force". More details on using APBS for the polar and nonpolar portions of such a cycle are given in the following sections.

Polar solvation

The full free energy cycle is usually decomposed into polar and nonpolar parts. The polar portion is usually represented by the charging energies in Steps 2 and 6:

$$\Delta_p G = \Delta_2 G - \Delta_6 G$$

Energies returned from APBS electrostatics calculations are charging free energies. Therefore, to calculate the polar contribution to the solvation free energy, we simply need to setup two calculations corresponding to Steps 2 and 6 in the free energy cycle. Note that the electrostatic charging free energies returned by APBS include self-interaction terms. These are the energies of a charge distribution interacting with itself. Such self-interaction energies are typically very

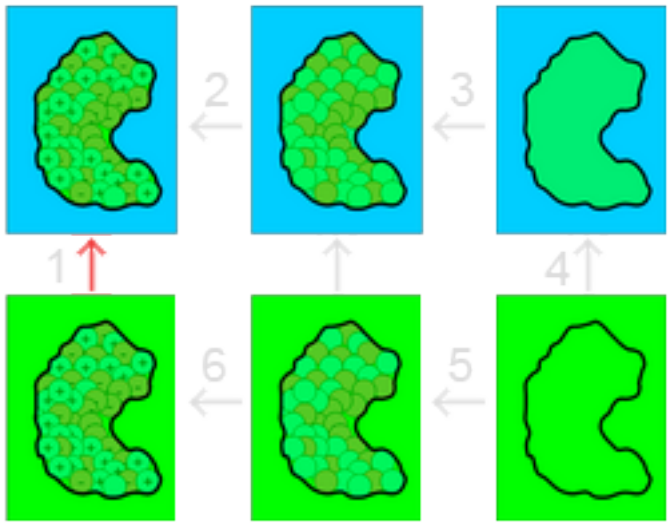


Fig. 9.1: Our model solvation free energy cycle illustrating several steps: 1. The solvation energy to be calculated. 2. Charging of the solute in solution (e.g., inhomogeneous dielectric, ions present). 3. Introduction of attractive solute-solvent dispersive interaction interactions (e.g., an integral of Weeks-Chandler-Andersen interactions over the solvent-accessible volume). 4. Introduction of repulsive solute-solvent interaction (e.g., cavity formation). 5. Basically a null step although it could be used to offset unwanted energies added in Steps 3 and 4 above. 6. Charging of the solute in a vacuum or homogeneous dielectric environment in the absence of mobile ions.

large and extremely sensitive to the problem discretization (grid spacing, location, etc.). Therefore, it is very important that the two calculations in Steps 2 and 6 are performed with identical grid spacings, lengths, and centers, in order to ensure appropriate matching (or "cancellation") of self-energy terms.

Born ion

One of the canonical examples for polar solvation is the Born ion: a nonpolarizable sphere with a single charge at its center surrounded by an aqueous medium. Consider the transfer of a non-polarizable ion between two dielectrics. In the initial state, the dielectric coefficient inside and outside the ion is ϵ_in, and in the final state, the dielectric coefficient inside the ion is ϵ_in and the dielectric coefficient outside the ion is ϵ_in. In the absence of external ions, the polar solvation energy of this transfer for this system is given by:

$$\Delta\_pG\_\mathrm{Born} = \frac{q^2}{8\pi\epsilon\_0 a}\left(\frac{1}{\epsilon\_\mathrm{out}} - \frac{1}{\epsilon\_\mathrm{in}}\right)$$

where q is the ion charge, a is the ion radius, and the two ϵ variables denote the two dielectric coefficients. This model assumes zero ionic strength.

Note that, in the case of transferring an ion from vacuum, where ϵ_in $= 1$, the expression becomes

$$\Delta\_pG\_\mathrm{Born} = \frac{q^2}{8\pi\epsilon\_0 a}\left(\frac{1}{\epsilon\_\mathrm{out}} - 1\right)$$

We can setup a PQR file for the Born ion for use with APBS with the contents:

```
REMARK  This is an ion with a 3 A radius and a +1 e charge
ATOM      1   I  ION     1 0.000   0.000   0.000  1.00 3.00
```

We're interested in performing two APBS calculations for the charging free energies in homogeneous and heterogeneous dielectric coefficients. We'll assume the internal dielectric coefficient is 1 (e.g., a vacuum) and the external

dielectric coefficient is 78.54 (e.g., water). For these settings, the polar Born ion solvation energy expression has the form

$$\Delta_p G_{\text{Born}} = -691.85\left(\frac{z^2}{R}\right)\text{kJ A/mol}$$

where z is the ion charge in electrons and R is the ion size in Å.

This solvation energy calculation can be setup in APBS with the following input file:

```
# READ IN MOLECULES
read
  mol pqr born.pqr
end
elec name solv # Electrostatics calculation on the solvated state
  mg-manual # Specify the mode for APBS to run
  dime 97 97 97 # The grid dimensions
  nlev 4 # Multigrid level parameter
  grid 0.33 0.33 0.33 # Grid spacing
  gcent mol 1 # Center the grid on molecule 1
  mol 1 # Perform the calculation on molecule 1
  lpbe # Solve the linearized Poisson-Boltzmann equation
  bcfl mdh # Use all multipole moments when calculating the potential
  pdie 1.0 # Solute dielectric
  sdie 78.54 # Solvent dielectric
  chgm spl2 # Spline-based discretization of the delta functions
  srfm mol # Molecular surface definition
  srad 1.4 # Solvent probe radius (for molecular surface)
  swin 0.3 # Solvent surface spline window (not used here)
  sdens 10.0 # Sphere density for accessibility object
  temp 298.15 # Temperature
  calcenergy total # Calculate energies
  calcforce no # Do not calculate forces
end
elec name ref # Calculate potential for reference (vacuum) state
  mg-manual
  dime 97 97 97
  nlev 4
  grid 0.33 0.33 0.33
  gcent mol 1
  mol 1
  lpbe
  bcfl mdh
  pdie 1.0
  sdie 1.0
  chgm spl2
  srfm mol
  srad 1.4
  swin 0.3
  sdens 10.0
  temp 298.15
  calcenergy total
  calcforce no
end
# Calculate solvation energy
print energy solv - ref end
quit
```

Running this example with a recent version of APBS should give an answer of -229.59 kJ/mol which is in good agreement with the -230.62 kJ/mol predicted by the analytic formula above.

Note: The Born example above can be easily generalized to other polar solvation energy calculations. For example, ions could be added to the solv ELEC, dielectric constants could be modified, surface definitions could be changed (in both ELEC sections!), or more complicated molecules could be examined. Many of the examples included with APBS also demonstrate solvation energy calculations.

Note: As molecules get larger, it is important to examine the sensitivity of the calculated polar solvation energies with respect to grid spacings and dimensions.

Apolar solvation

Referring back to the solvation free energy cycle, the nonpolar solvation free energy is usually represented by the energy changes in Steps 3 through 5:

$$\Delta_n G = (\Delta_3 G - \Delta_5 G) + \Delta_4 G$$

where Step 4 represents the energy of creating a cavity in solution and Steps 3-5 is the energy associated with dispersive interactions between the solute and solvent. There are many possible choices for modeling this nonpolar solvation process. APBS implements a relatively general model described by Wagoner and Baker (2006) and references therein. The implementation and invocation of this model is described in more in the *APOLAR input file section* documentation. Our basic model for the cavity creation term (Step 4) is motivated by scaled particle theory and has the form

$$\Delta_4 G = pV + \gamma A$$

where p is the solvent pressure (*press* keyword), V is the solute volume, γ is the solvent surface tension (*gamma* keyword), and A is the solute surface area.

Our basic model for the dispersion terms (Steps 3 and 5) follow a Weeks-Chandler-Anderson framework as proposed by Levy et al (2002):

$$\Delta_3 G - \Delta_5 G = \bar{\rho} \int_{\omega} u^{(att)}(y)\theta(y)dy$$

where $\overline{\rho}$ is the bulk solvent density (*bconc* keyword), Ω is the problem domain, $u^{(\mathrm{att})}(y)$ is the attractive dispersion interaction between the solute and the solvent at point y with dispersive Lennard-Jones parameters specified in APBS parameter files, and $\theta(y)$ describes the solvent accessibility of point y.

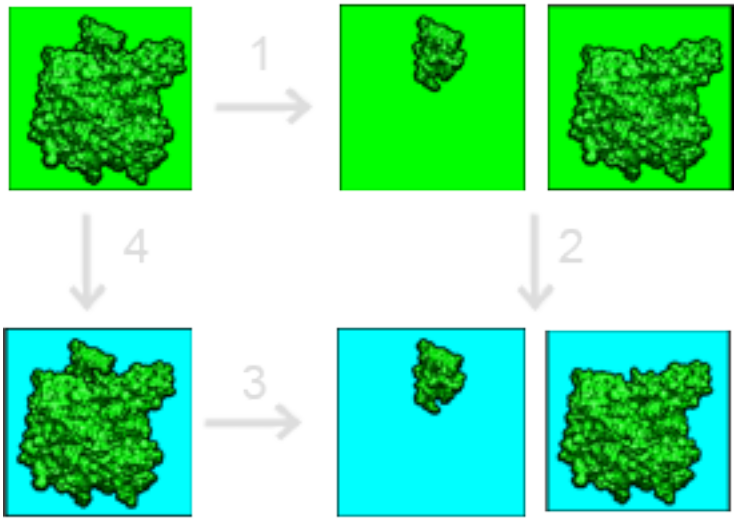
The ability to independently adjust *press*, *gamma*, and *bconc* means that the general nonpolar solvation model presented above can be easily adapted to other popular nonpolar solvation models. For example, setting *press* and *bconc* to zero yields a typical solvent-accessible surface area model.

Binding energies with APBS

In general, implicit solvent models are used to calculation the contribution of solvation to binding free energies. Additional binding free energy contributions (molecular mechanics energies, entropic changes, etc.) must be calculated separately and are not discussed in this tutorial.

Free energy cycle

Our framework for calculating solvation contributions to binding free energies is shown in the figure below:



This binding free energy cycle illustrates binding in terms of transfer free energies from a homogeneous dielectric environment (where interactions are described by Coulomb's law) to an inhomogeneous dielectric environment with differing internal (green) and external (cyan) dielectric constants. The binding (dissociation) free energy is depicted in Step 3. The binding free energy is given by

$$\Delta_b G = -\Delta_3 G = \Delta_4 G - \Delta_1 G - \Delta_2 G.$$

The following sections provide more detail on calculating individual terms of this equation.

Binding energy calculations

The most general method for calculating binding free energies divides the binding process up into solvation $\Delta\Delta_s G$ and Coulombic $\Delta\Delta_c G$ components:

$$\Delta\Delta_b G = \Delta\Delta_s G + \Delta\Delta_c G.$$

As mentioned above, this framework neglects the numerous other mechanical and entropic components actually involved in the binding process.

Solvation contribution to binding

If we're just interested in calculating the solvation contributions to binding (steps 4 and 2 in the binding free energy cycle), then we simply need to follow the instructions from the *Solvation energies with APBS* section for the complex and isolated components. The solvation energy contribution to the binding is then given by

$$\Delta\Delta_s G = \Delta_4 G - \Delta_2 G = \Delta_s G_{cmpx} - \Delta_s G_{mol1} - \Delta_s G_{mol2}$$

Coulombic contribution to binding

To complete the binding free energy cycle, we need to add intermolecular Coulombic contributions to the solvation energy change upon binding to get the total electrostatic/solvent contribution to the binding free energy. In particular, we're interested in the change in Coulombic electrostatic energy upon binding, as given by

$$\Delta\Delta_c G = -\Delta_1 G = \Delta_c G_{cmpx} - \Delta_c G_{mol1} - \Delta_c G_{mol2}$$

Each of the quantities in this equation is the sum of pairwise Coulombic interactions between all atoms in the molecule (or complex) for a particular uniform dielectric. In order to combine these Coulombic binding energies with the solvation energies described above, we need to make sure consistent dielectric constants are used. In particular, Coulombic interactions should be calculated using the same uniform dielectric constant as the reference state of the solvation energy above. For example, if solvation energies are calculated for transferring a protein from a homogeneous medium with uniform dielectric of to an inhomogeneous medium with internal dielectric ϵ_u and external dielectric ϵ_v, then Coulombic energies should be calculated using a dielectric of ϵ_u. The APBS accessory program `tools/manip/coulomb` was created to help with the calculation of these analytic individual per-molecule Coulombic energies. Given a PQR file as input, the `tools/manip/coulomb` program calculates Coulombic energies for a vacuum dielectric (e.g., a uniform dielectric of 1). If the reference dielectric is ϵ_u, then all energies returned by `tools/manip/coulomb` need to be divided by ϵ_u.

Other examples

Several binding energy examples are distributed in the `examples` directory with APBS.

Todo

Link binding energy examples directly from the source tree.

Protein-RNA binding linked equilibria

Before reading this example, please review *Caveats and sources of error* for relevant caveats.

Introduction

This example is taken from a paper by García-García and Draper. Special thanks to David Draper who provided the PDB files. This example explores the electrostatic contributions to the binding interaction between a 22-residue α-helical peptide of protein λ with the "box B" RNA hairpin structure. In particular, this example uses nonlinear Poisson-Boltzmann equation calculations to look at the non-specific screening effects of monovalent salt on the peptide-RNA complex. García-García and Draper isolated the contribution of KCl concentration to the binding of the folded peptide with the folded RNA hairpin and determined a fairly linear relationship between the binding free energy $\Delta_b G$ and the logarithm of the KCl concentration which yields

$$\frac{\partial \Delta_b G}{\partial \log_{10}[\mathrm{KCl}]} = 6.0 \pm 0.2 \text{ kcal/mol}$$

This slope can be used to determine the number of KCl ions linked to the binding equilibrium through the expression

$$n = -\frac{\partial \Delta_b G}{RT \partial \log_{10}[\mathrm{KCl}]} = -4.52 \pm 0.08 \text{ kcal/mol}$$

where RT is the thermal energy, to determine $n = -4.4 \pm 0.2$ for the RNA-peptide binding equilibrium. RT is equal to $kT * N_a$ where kT is the product of the Boltzmann constant k (equal to the gas constant R/N_a), and the temperature T (at STP it is 298.15 K) and N_a is Avogadro's constant. Thus RT is equal to

$$R \text{ (Joules/Kelvin)} * T \text{ (Kelvin)} * N_a \text{ (mols)} * 1 \text{ kJ/1000 J}$$

which roughly equals

$$(1.38 \times 10^{-23}) \times (6.022 \times 10^{23}) \times (298.15)/(1000)$$

which is approximately 2.479 kJ/mol or 0.593 kcal/mol.

García-García and Draper used nonlinear Poisson-Boltzmann equation calculations to estimate the electrostatic contributions to the binding free energy as a function of the monovalent salt concentration. As *discussed elsewhere*, the Poisson-Boltzmann equation is only able to describe non-specific interactions of ions with solutes, including the effects of ion size and charge but otherwise ignoring the important differences between ionic species. Interestingly (and perhaps surprisingly), they find excellent agreement between the experimental binding energy dependence on KCl and their Poisson-Boltzmann calculations with equivalent concentrations of monovalent ions. This agreement strongly suggests that the binding of RNA and the peptide is primarily determined by electrostatic interactions. It also suggests that the primary interaction of the KCl with this system is through non-specific screening interactions. The García-García and Draper nonlinear Poisson-Boltzmann equation calculations gave:

$$\frac{\partial \Delta_b G}{\partial \log_{10}[\mathrm{KCl}]} = 5.9 \pm 0.2 \text{ kcal/mol}$$

and $n = -4.3 \pm 0.2$ for KCl linkage to the RNA-peptide binding equilibrium.

APBS implementation

This example follows the calculations from their paper.

The PQR files are included in the `examples/protein-rna/` directory of the apbs-pdb2pqr repository. This directory also includes a `template.txt` file that serves as a template for the APBS input files with `IONSTR` as a placeholder for the ionic strength. This file is also shown here:

```
read
  mol pqr model_outNB.pqr
  mol pqr model_outNpep.pqr
  mol pqr model_outBoxB19.pqr
end
elec name complex
  mg-auto
  dime 65 97 129
  cglen 45.3322 54.9498 82.2633
  fglen 45.3322 52.3234 68.3902
  cgcent mol 1
  fgcent mol 1
  mol 1
  npbe
  bcfl sdh
  pdie 4.0
  ion charge 1 conc IONSTR radius 2.0
  ion charge -1 conc IONSTR radius 2.0
  sdie 80.0
  srfm mol
  chgm spl2
  sdens 10.00
  srad 1.40
  swin 0.30
  temp 298.15
  calcenergy total
  calcforce no
  write qdens dx qdens-complex-IONSTR
  write ndens dx ndens-complex-IONSTR
end
elec name peptide
  mg-auto
  dime 65 97 129
  cglen 45.3322 54.9498 82.2633
```

```
  fglen 45.3322 52.3234 68.3902
  cgcent mol 1
  fgcent mol 1
  mol 2
  npbe
  bcfl sdh
  pdie 4.0
  sdie 80.0
  ion charge 1 conc IONSTR radius 2.0
  ion charge -1 conc IONSTR radius 2.0
  srfm mol
  chgm spl2
  sdens 10.00
  srad 1.40
  swin 0.30
  temp 298.15
  calcenergy total
  calcforce no
  write qdens dx qdens-peptide-IONSTR
  write ndens dx ndens-peptide-IONSTR
end
elec name rna
  mg-auto
  dime 65 97 129
  cglen 45.3322 54.9498 82.2633
  fglen 45.3322 52.3234 68.3902
  cgcent mol 1
  fgcent mol 1
  mol 3
  npbe
  bcfl sdh
  pdie 4.0
  sdie 80.0
  ion charge 1 conc IONSTR radius 2.0
  ion charge -1 conc IONSTR radius 2.0
  srfm mol
  chgm spl2
  sdens 10.00
  srad 1.40
  swin 0.30
  temp 298.15
  calcenergy total
  calcforce no
  write qdens dx qdens-rna-IONSTR
  write ndens dx ndens-rna-IONSTR
end
print elecEnergy complex - peptide - rna end
quit
```

As used in the template file, the READ command, our calculation will have three parts:

- Calculation of the total electrostatic energy (including self-interaction energies) of the peptide-RNA complex. This calculation is named complex in the input file.
- Calculation of the total electrostatic energy (including self-interaction energies) of the peptide. This calculation is named peptide in the input file.
- Calculation of the total electrostatic energy (including self-interaction energies) of the RNA. This calculation is named rna in the input file.

The calculations themselves will not be overly demanding, since we will use relatively coarse grids. This grid coarseness has a significant impact on the absolute electrostatic binding energy we obtain from this particular calculation: the calculated energy isn't converged with respect to grid spacing. However, the overall slope of binding energy with respect to monovalent ion concentration is rather insensitive with respect to the grid spacing, allowing us to save computational time and effort during the calculations. The calculation will conclude with a *PRINT input file section* command which will combine the total energies from the three parts to obtain our approximate absolute electrostatic binding energy for the complex at 0.225 M monovalent salt concentration. It is very important to note that this absolute energy no meaning in isolation for several reasons:

- It is not converged with respect to grid spacing
- It does not contain other very important non-electrostatic aspects of the binding energy which are important for the measured affinity

`IONSTR` is a placeholder that represents the ion concentration for the APBS calculation.

You will also have to create a `dxmath.txt` file which contains the following.

```
qdens-complex-IONSTR.dx
qdens-pep-IONSTR.dx -
qdens-rna-IONSTR.dx -
qdens-diff-IONSTR.dx =
```

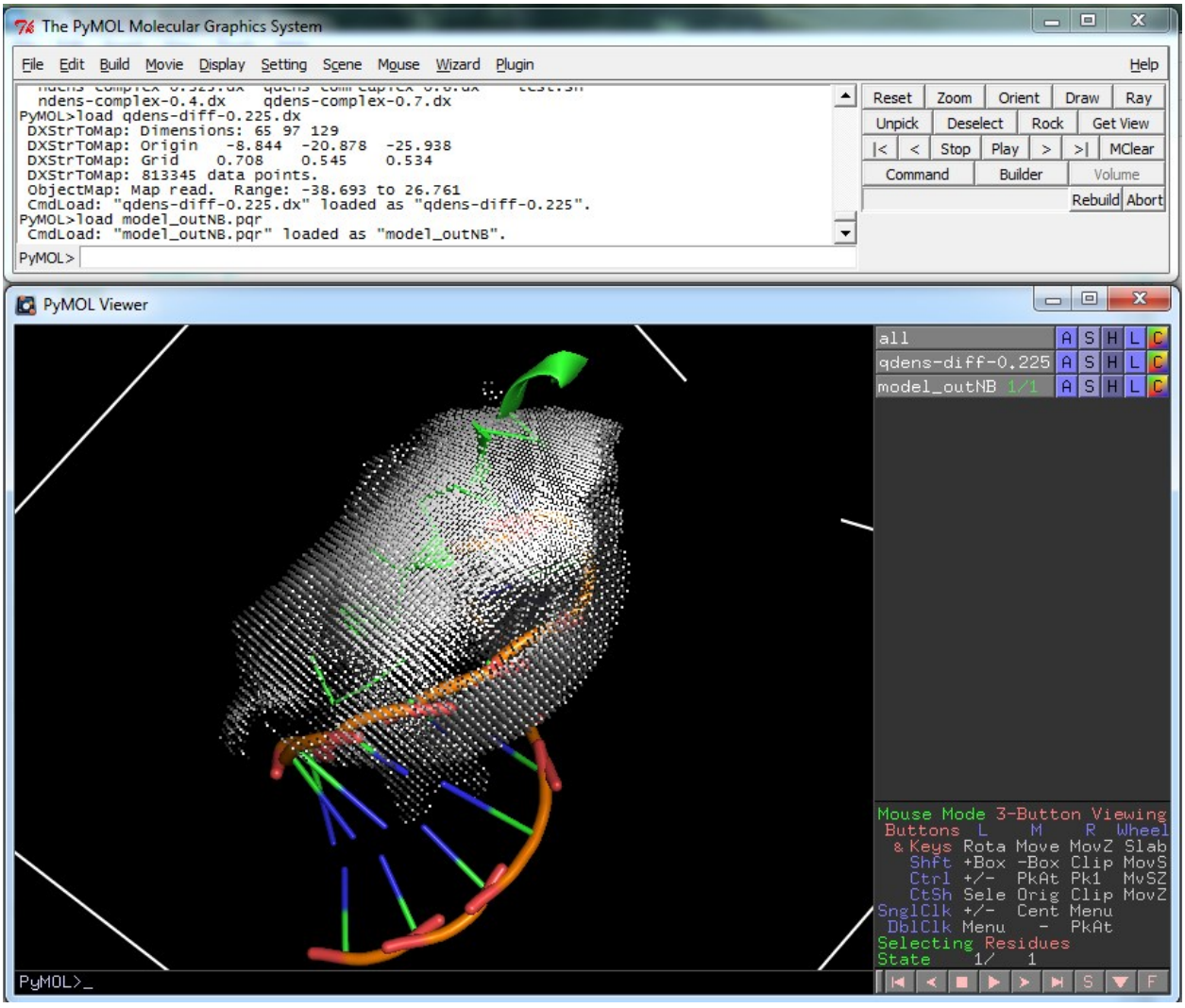
dxmath will subtract the dx maps of the individual peptide and RNA from the overall structure (and prints to the `qdens-diff-IONSTR.dx` file.

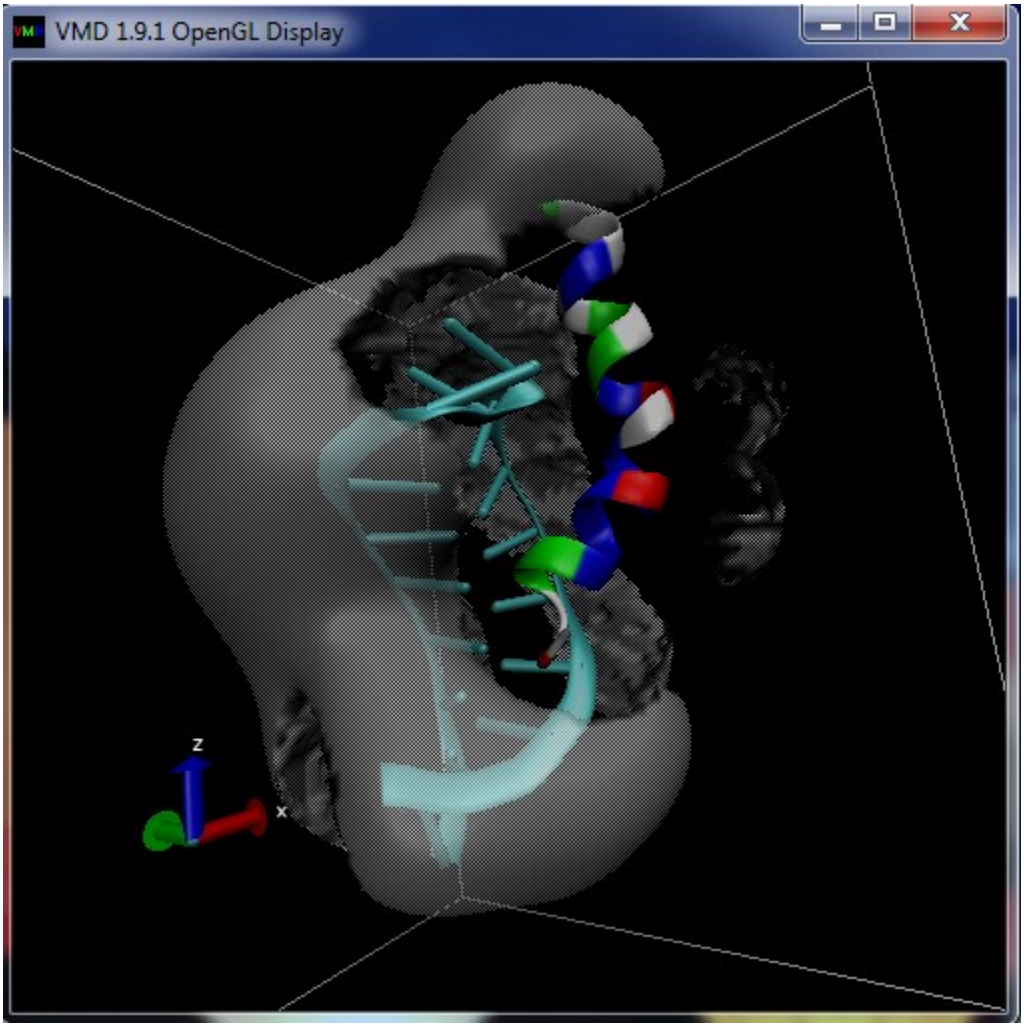
Automation with Python

We have provided Python scripts `apbs_win, unix_dx.py` that run the necessary APBS calculations and analyze the results. When you run these programs, you need to be in the same directory as `template.txt` and `dxmath.txt`. This script will create all the input files for the tests as well as run apbs and dxmath on your `template.txt` and `dxmath.txt` files. Most of the syntax fills in the ion concentrations in the template file, and the call commands actually run the calculations on each input.

Visualization

The `qdens-diff-0.225.dx` file produced by the script can be viewed in PyMOL or another visualization program to give something similar to the following imaged which show the difference in charge density before and after binding.


The PyMOL Molecular Graphics System
File Edit Build Movie Display Setting Scene Mouse Wizard Plugin Help
ndens-complex-0.4.dx qdens-complex-0.7.dx
PyMOL>load qdens-diff-0.225.dx
DXStrToMap: Dimensions: 65 97 129
DXStrToMap: Origin -8.844 -20.878 -25.938
DXStrToMap: Grid 0.708 0.545 0.534
DXStrToMap: 813345 data points.
ObjectMap: Map read. Range: -38.693 to 26.761
CmdLoad: "qdens-diff-0.225.dx" loaded as "qdens-diff-0.225".
PyMOL>load model_outNB.pqr
CmdLoad: "model_outNB.pqr" loaded as "model_outNB".
PyMOL>
Reset Zoom Orient Draw Ray
Unpick Deselect Rock Get View
|< < Stop Play > >| MClear
Command Builder Volume
Rebuild Abort
PyMOL Viewer
all A S H L C
qdens-diff-0.225 A S H L C
model_outNB 1/1 A S H L C
Mouse Mode 3-Button Viewing
Buttons L M R Wheel
& Keys Rota Move MovZ Slab
Shft +Box -Box Clip MovS
Ctrl +/- PkAt Pk1 MvSZ
CtSh Sele Orig Clip MovZ
SnglClk +/- Cent Menu
DblClk Menu - PkAt
Selecting Residues
State 1/ 1
PyMOL>_



Parallel APBS execution for large calculations

Why parallel?

APBS finite difference multigrid calculations require approximately 200 B memory per grid point. These memory requirements can be distributed in two ways during a calculation:

- APBS calculations can be performed in parallel across multiple processors (hopefully, sharing distributed memory!). This functionality is provided by using the *mg-para* keyword.
- APBS calculations can be broken into a series of smaller, asynchronous runs which (individually) require less memory. This functionality is provided by using both the *mg-para* and *async* keywords.

Synchronous parallel calculations

The actin dimer example provided with the APBS distribution `examples/actin-dimer/` is a fairly large system that can often require too much memory for some systems. This example will use the actin dimer complex PQR file (`complex.pqr`) to illustrate parallel focusing.

We're going to use an 8-processor parallel calculation to write out the electrostatic potential map for this complex. Each processor will solve a portion of the overall problem using the parallel focusing method on a 973 mesh with 20%

overlap between meshes for neighboring processors. An example input file for this calculation might look like:

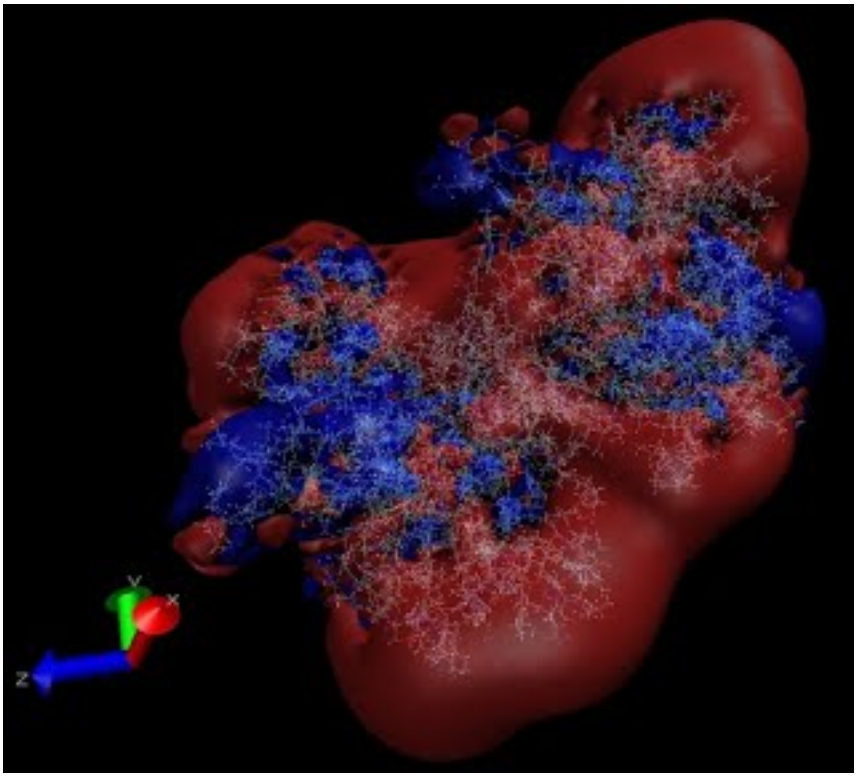
```
read
  mol pqr complex.pqr
end
elec name complex
  mg-para
  ofrac 0.1
  pdime 2 2 2
  dime 97 97 97
  fglen 150 115 160
  cglen 156 121 162
  cgcent mol 1
  fgcent mol 1
  mol 1
  npbe
  bcfl sdh
  ion 1 0.150 2.0
  ion -1 0.150 2.0
  pdie 2.0
  sdie 78.54
  srfm mol
  chgm spl0
  srad 1.4
  swin 0.3
  sdens 10.0
  temp 298.15
  calcenergy total
  calcforce no
  write pot dx pot
end
quit
```

where the "*pdime* 2 2 2" statement specifies the 8-processor array dimensions, the "*ofrac* 0.1" statement specifies the 20% overlap between processor calculations, and the "*dime* 97 97 97' statement specifies the size of each processor's calculation. The "*write* pot dx potential" instructs APBS to write out OpenDX-format maps of the potential to 8 files `potential-#.dx`, where # is the number of the particular processor.

An MPI-compiled version of APBS can be used with this input file to run 8 parallel focusing calculations, with each calculation generating fine-scale solutions on a different region of the (*fglen*) problem domain. Note that 8 separate OpenDX files are written by the 8 processors used to perform the calculation. Writing separate OpenDX< files allows us to avoid communication in the parallel run and keeps individual file sizes (relatively) small. Additionally, if a user is interested in a specific portion of the problem domain, only a few files are needed to get local potential information. However, most users are interested in global potentials. APBS provides the *mergedx and mergedx2* program to reassemble the separate OpenDX files into a single file. *mergedx* is a simple program that allows users to combine several OpenDX files from a parallel focusing calculation into a single map. This map can be down-sampled from the original resolution to provide coarser datasets for fast visualization, etc. For example, the command

```
$ mergedx 65 65 65 pot0.dx pot1.dx pot2.dx pot3.dx pot4.dx pot5.dx pot6.dx pot7.dx
```

will generate a file `gridmerged.dx` which has downsampled the much larger dataset contained in the 8 OpenDX files into a 65^3 file which would be suitable for rough visualization. An example of mergedx output visualization is shown in the attached figure. Note that downsampling isn't necessary – and often isn't desirable for high quality visualization or quantitative analysis.



Asynchronous parallel calculations

The steps described in the previous section can also be performed for systems or binaries which are not equipped for parallel calculations via MPI. In particular, you can add the statement "*async n*" to the ELEC *mg-para* section of the APBS input file to make the single-processor calculation masquerade as processor *n* of a parallel calculation.

Scalar maps from asynchronous APBS calculations can be combined using the mergedx program as described above. Currently, energies and forces from asynchronous APBS calculations need to merged manually (e.g., summed) from the individual asynchronous calculation output. This can be accomplished by simple shell scripts.

Todo

Migrate geoflow, pbsam, pbam examples over from `examples` directory.

Visualizing results

There are several programs available for visualizing APBS results. The easiest is the PDB2PQR web server which provides *3Dmol.js* <*http://3dmol.csb.pitt.edu/*> and *Jmol* <*http://jmol.sourceforge.net/*> browser-based visualization capabilities.

Other programs include:

- PyMOL
- VMD
- PMV

- Chimera

Using the PyMOL APBS plugin

The PyMOL molecular graphics software package can both run APBS and visualize resulting electrostatic potentials. Below are instructions for performing a basic demonstration of how to go from a PDB entry to a plot of structure and potential in PyMOL using APBS.

Run the APBS calculation

- Load your PQR file you created into PyMOL (*File* → *Open...*) and choose your favorite graphical representation of the molecular structure.
- Go to *Plugin* → *APBS Tools...* to open the APBS calculation plugin.
- Under the *Main* tab of the PyMOL APBS Tools window, select *Use another PQR* and either browse to (via the *Choose Externally Generated PQR* button) or input the path to your PQR file. This step is necessary to ensure you use the radii and charges assigned by PDB2PQR.
- Under the *APBS Location* tab of the PyMOL APBS Tools window, either browse to (via the APBS binary location: button) or input the path to your local APBS binary. It is not necessary to provide a path to the APBS `psize.py` binary for most biomolecules.
- Under the *Temporary File Locations* tab of the PyMOL APBS Tools window, customize the locations of the various temporary files created during the run. This can be useful if you want to save the generated files for later use.
- Under the *Configuration* tab of the PyMOL APBS Tools window, press *Set grid* to set the grid spacings. The default values are usually sufficient for all but the most highly charged biomolecules.
- Under the *Configuration* tab of the PyMOL APBS Tools window, customize the remaining parameters; the defaults are usually OK.

Note: 0.150 M concentrations for the +1 and 1 ion species are often useful to ensure that electrostatic properties are not overly exaggerated.

- Under the *Configuration* tab of the PyMOL APBS Tools window, press the Run *APBS button* to start the APBS calculation. Depending on the speed of your computer, this could take a few minutes. The *Run APBS* button will become unselected when the calculation is finished.

Visualize the results

Before proceeding, you must load the electrostatic potential data into PyMOL. Under the *Visualization* tab of the PyMOL APBS Tools window, press the *Update* button.

Electrostatic isocontours

PyMOL makes this step very easy: adjust the positive and negative "Contour" fields to the desired values (usually ± 1, ± 5, or ± 10 kT/e) and press the *Positive Isosurface*, *Negative Isosurface*, and *Show buttons*.

At this point, you probably have a figure that looks something like the image below.

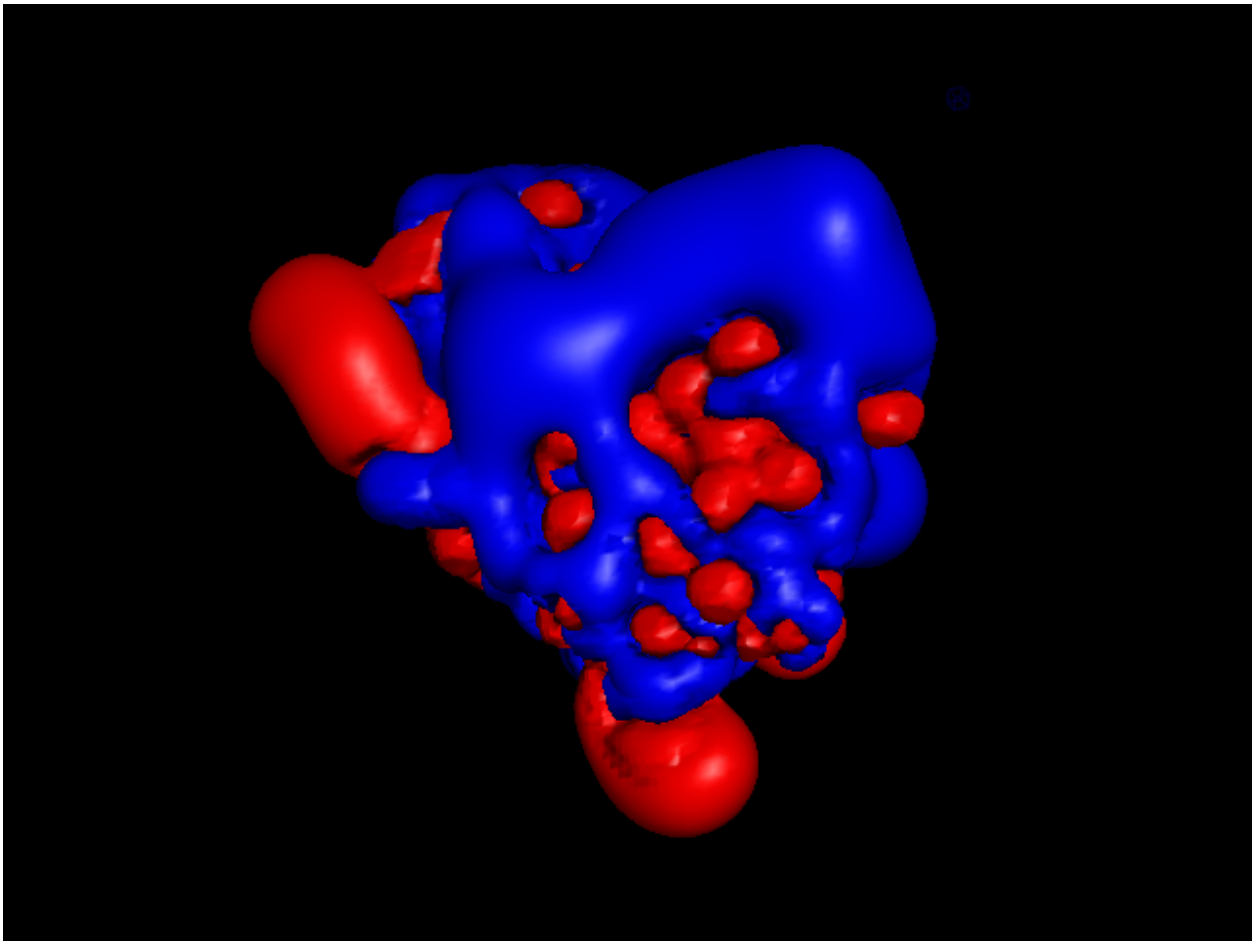


Fig. 9.2: ± 1 kT/e electrostatic potential isocontours of FAS2 in PyMOL

If the colors are not as you expect, you can change the colors of the objects iso_neg and iso_pos in the main menu. By convention (for electrostatics in chemistry), red is negative (think oxygen atoms in carboxyl groups) and blue positive (think nitrogen atoms in amines).

Surface potentials

If you haven't already, hide the isocontours by pressing the *Positive Isosurface*, *Negative Isosurface*, and *Hide* buttons. The surface potential is also straightforward to visualize. Set the "Low" and "High"values to the desired values (usually ± 1, ± 5, or ± 10 kT/e) at which the surface colors are clamped at red (-) or blue (+). Check the "Solvent accessible surface" and "Color by potential on sol. acc. surf." buttons to plot the potential on the solvent-accessible (probe-inflated or Lee-Richards) surface. Press the *Molecular Surface Show* button to load the surface potential.

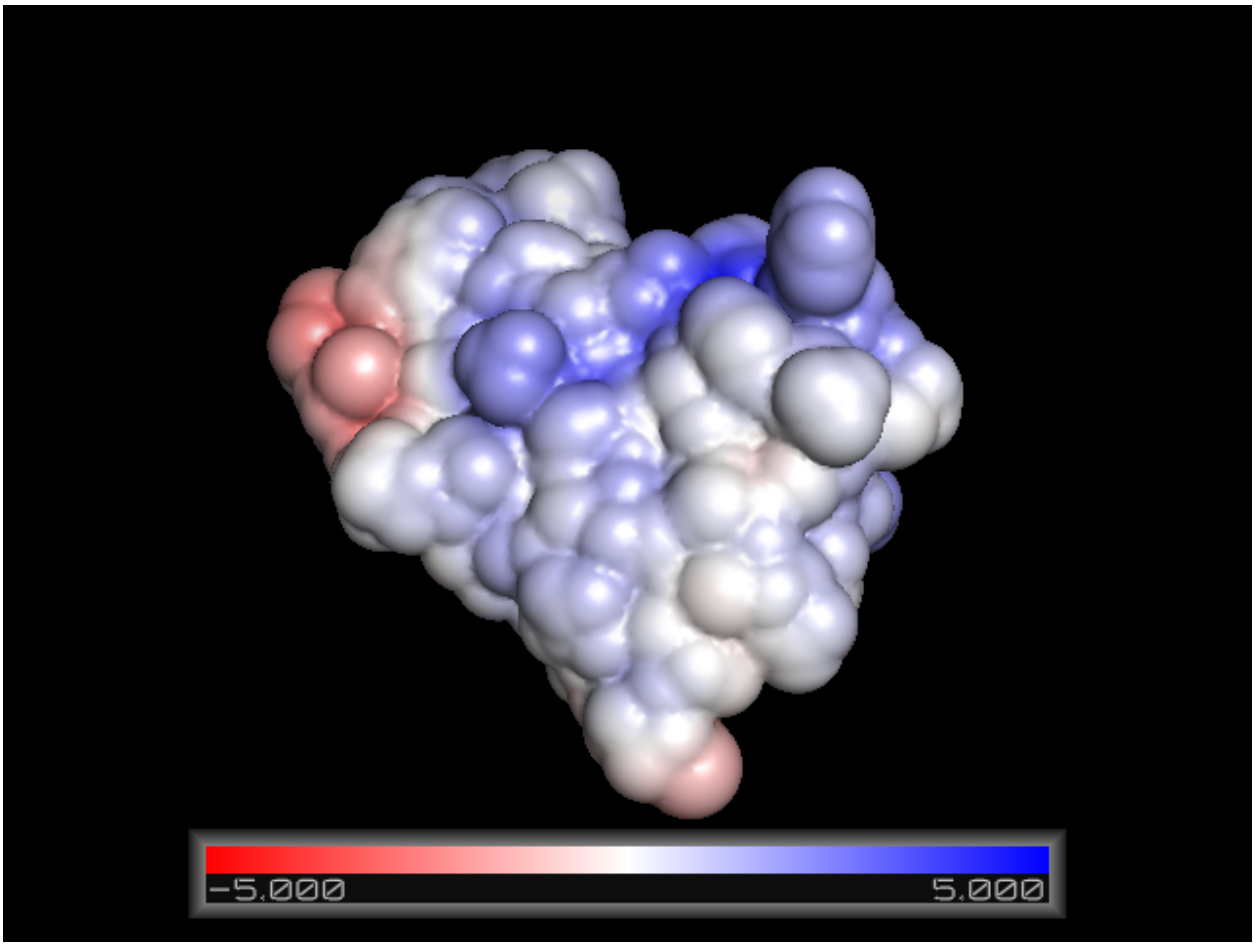


Fig. 9.3: ± 5 kT/e electrostatic potential of FAS2 in PyMOL plotted on the solvent-accessible surface.

The solvent-accessible surface tends to reveal more global features of the surface potential. Tighter surfaces (e.g., van der Waals and molecular or Connolly surfaces) provide more information about the shape of the biomolecule but otherwise tend to simply map atomic surface charges onto the biomolecular surface. PyMOL can simultaneously provide geometric information (from the molecular surface) and useful electrostatic potential information (from the solvent-accessible surface). To visualize the molecule in this way, simply uncheck the "Solvent accessible surface"box and check the "Color by potential on sol. acc. surf." box on the *Visualization* tab.

Virtual reality with UnityMol

Molecular visualization software packages provide the ability for users to explore the 3D representations molecular structures and properties. Typical user interaction is limited to panning, zooming, and rotating the molecule using a mouse and keyboard while viewing on a standard computing monitor. These techniques support a pseudo 3-dimensional view of a molecule to understand its structure but lack the true depth perception people are used to with stereoscopic vision in the real world.

New advancements in virtual reality (VR) technologies has resulted in lower costs and systems that are easier to use to many consumers. Compared to past VR hardware, these new systems have several key advancements including lower latency, higher frame rates, and improved resolution. Additionally, these systems are equipped with better optics and motion tracking and a more robust software ecosystem.

We are extending the visualization capabilities for APBS through the incorporation of a VR device with molecular rendering software. We are currently experimenting with the HTC Vive, which allows a person to walk around a 15' by 15' physical space while wearing a head mounted display. Precise head movements are matched in virtual reality with no noticeable latency. Additionally, the HTC Vive controllers are motion tracked with millimeter precision and provide a valuable method for interacting with virtual objects. We have enabled VR using the HTC Vive in the UnityMol molecular visualization software (created by Baaden, et al.) and incorporated electrostatic surface data (see figure below and a YouTube video). New viewing capabilities now include walking around, grabbing (using the motion controllers), and scaling (gestures) of molecules. We are actively working with Dr. Baaden and his group to determine the best use of interaction techniques for users to interact with molecular models through his software.

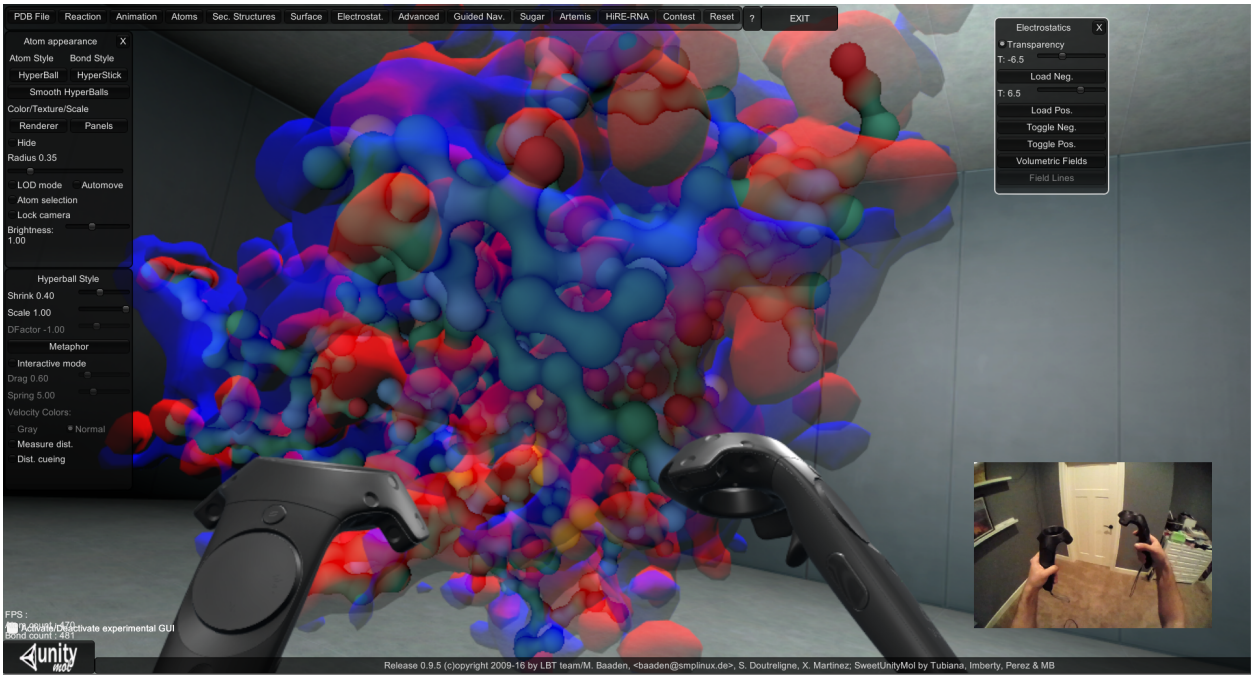


Fig. 9.4: View of UnityMol form the monitor as it is being used in VR with controllers.

For future work, we would like to further extend UnityMol in the HTC Vive to include natural user interactions for viewing multiple molecules, vary the electrostatic results from APBS, and change molecular attributes. We envision this tool will also enable virtual collaboration for participant in different locations. Each participant will be able to view, gesture and interact with the same data in the same VR space. Finally, we would like to explore the use of VR for research related to docking of different molecules.

Todo

Add VMD tutorial.

CHAPTER 10

Support for APBS-PDB2PQR

Supporting organizations

A special thanks supporting organizations behind the APBS and PDB2PQR software:

National Institutes of Health Primary source of funding for APBS via grant GM069702

National Biomedical Computation Resource Deployment and computational resources support

National Partnership for Advanced Computational Infrastructure Funding and computational resources

Washington University in St. Louis Start-up funding

Please support us by registering

Please help ensure continued support for APBS-PDB2PQR by registering your use of our software.

Contributors to date

Contributions to the APBS and PDB2PQR are always welcome and can be shared through GitHub] or our other supprot mechanisms (see *Getting help*).

The following is an alphabetical list of contributors to the APBS/PDB2PQR effort:

- Nathan Baker: APBS, PDB2PQR
- Tucker Beck: APBS
- Steve Bond: APBS
- Juan Brandi: APBS, PDB2PQR
- Larry Canino: APBS

- Juahui Chen: APBS
- Zhan Chen: APBS
- Minju Chun: PDB2PQR
- Vincent Chu: APBS
- Todd Dolinsky: APBS, PDB2PQR
- Adrian Elcock: APBS
- Lisa Felberg: APBS
- Weihua Geng: APBS
- Dave Gohara: APBS
- Michael Grabe: APBS
- Stephen Gradwohl: APBS
- Tyler Harmon: APBS
- Teresa Head-Gordon: APBS
- Yong Huang: APBS, PDB2PQR
- Michael Holst: APBS
- Peter Hui: APBS
- Jan Jensen: PDB2PQR
- Liz Jurrus: APBS, PDB2PQR
- Adrian Kaats: APBS
- Patrice Koehl: APBS
- David Koes: PDB2PQR
- Robert Konecny: APBS, PDB2PQR
- Robert Krasny: APBS
- Max Li: APBS
- Peter Li: PDB2PQR
- Stephen Libby: APBS
- Chiansan Ma: APBS, PDB2PQR
- J Andrew McCammon: APBS, PDB2PQR
- Kyle Monson: APBS, PDB2PQR
- Jens Nielsen: PDB2PQR
- Jay Ponder: APBS
- Mike Schnieders: APBS
- Dave Sept: APBS, PDB2PQR
- Keith Star: APBS, PDB2PQR
- Andrew Stevens: APBS
- Samir Unni: APBS, PDB2PQR

- Guowei Wei: APBS
- Leighton Wilson: APBS
- Justin Xiang: APBS

This list is always out of date. Please email nathanandrewbaker@gmail.com with corrections.

CHAPTER 11

Citing your use of our software

- Please acknowledge your use of PDB2PQR by citing:
  - Dolinsky TJ, Czodrowski P, Li H, Nielsen JE, Jensen JH, Klebe G, Baker NA. PDB2PQR: Expanding and upgrading automated preparation of biomolecular structures for molecular simulations. Nucleic Acids Res, 35, W522-5, 2007. http://nar.oxfordjournals.org/content/35/suppl_2/W522
  - Dolinsky TJ, Nielsen JE, McCammon JA, Baker NA. PDB2PQR: an automated pipeline for the setup, execution, and analysis of Poisson-Boltzmann electrostatics calculations. Nucleic Acids Res, 32, W665-W667, 2004. http://nar.oxfordjournals.org/content/32/suppl_2/W665.abstract
- Please acknowledge your use of PEOE_PB protein/ligand parameterization software by citing:
  - Czodrowski P, Dramburg I, Sotriffer CA, Klebe G. Development, validation, and application of adapted PEOE charges to estimate pKa values of functional groups in protein-ligand complexes. Proteins, 65, 424-437, 2006. [(Link)](http://onlinelibrary.wiley.com/doi/10.1002/prot.21110/abstract;jsessionid=90CBD709146173D81A0F7554C256C01A.f01t02)
- Please acknowledge your use of APBS by citing:
  - Baker NA, Sept D, Joseph S, Holst MJ, McCammon JA. Electrostatics of nanosystems: application to microtubules and the ribosome. Proc. Natl. Acad. Sci. USA 98, 10037-10041 2001. http://www.pnas.org/content/98/18/10037
  - Additional articles discussing APBS and the PBE are available from the [suggested reading]
- Please acknowledge your use of the Holst group software by citing:
  - For the multigrid solver:
    - 13. Holst and F. Saied, Multigrid solution of the Poisson-Boltzmann equation. J. Comput. Chem. 14, 105-113, 1993.
    - 13. Holst and F. Saied, Numerical solution of the nonlinear Poisson-Boltzmann equation: Developing more robust and efficient methods. J. Comput. Chem. 16, 337-364, 1995.
  - For the finite element solver:
    - 13. Holst, Adaptive numerical treatment of elliptic systems on manifolds. Advances in Computational Mathematics 15, 139-191, 2001 http://dx.doi.org/10.1023/A:1014246117321

* 18. Bank and M. Holst, A New Paradigm for Parallel Adaptive Meshing Algorithms. SIAM Review 45, 291-323, 2003. http://epubs.siam.org/doi/abs/10.1137/S0036144503420061

CHAPTER 12

Suggested reading for APBS-PDB2PQR

- General solvation reviews
  - Baker NA. Poisson-Boltzmann methods for biomolecular electrostatics. Methods in Enzymology, 383, 94-118, 2004. http://www.sciencedirect.com/science/article/pii/S0076687904830052
  - Baker NA, McCammon JA. Electrostatic interactions. Structural Bioinformatics. Weissig H, Bourne PE, eds., 2005. http://dx.doi.org/10.1002/0471721204.ch21
  - Baker NA. Biomolecular applications of Poisson-Boltzmann methods. Reviews in Computational Chemistry. Lipkowitz KB, Larter R, Cundari TR., 21, 2005. http://dx.doi.org/10.1002/0471720895.ch5
  - Baker NA. Improving implicit solvent simulations: a Poisson-centric view. Curr Opin Struct Biol, 15, 137-43, 2005. http://dx.doi.org/10.1016/j.sbi.2005.02.001
  - Baker NA, Bashford D, Case DA. Implicit solvent electrostatics in biomolecular simulation. New Algorithms for Macromolecular Simulation. Leimkuhler B, Chipot C, Elber R, Laaksonen A, Mark A, Schlick T, Schutte C, Skeel R, eds., 2006. http://dx.doi.org/10.1007/3-540-31618-3_15
  - Dong F, Olsen B, Baker NA. Computational Methods for Biomolecular Electrostatics. Methods in Cell Biology: Biophysical Tools for Biologists, 84, 843-870, 2008. http://www.sciencedirect.com/science/article/pii/S0091679X0784026X
  - Ren P, Chun J, Thomas DG, Schnieders MJ, Marucho M, Zhang J, Baker NA. Biomolecular electrostatics and solvation: a computational perspective. Quart Rev Biophys, 45 (4), 427-491, 2012. http://dx.doi.org/10.1017/S003358351200011X
- APBS parallel multigrid solver
  - Baker NA, Sept D, Joseph S, Holst MJ, McCammon JA. Electrostatics of nanosystems: application to microtubules and the ribosome. Proc Natl Acad Sci USA, 98, 10037-41, 2001. http://dx.doi.org/10.1073/pnas.181342398
- APBS parallel finite element solver
  - Holst M, Baker NA, Wang F. Adaptive multilevel finite element solution of the Poisson-Boltzmann equation I: algorithms and examples. J Comput Chem, 21, 1319-42, 2000. http://bit.ly/1goFAFE

  - Baker N, Holst M, Wang F. Adaptive multilevel finite element solution of the Poisson-Boltzmann equation II: refinement schemes based on solvent accessible surfaces. J Comput Chem, 21, 1343-52, 2000. http://bit.ly/1dNSP8l
  - Baker NA, Sept D, Holst MJ, McCammon JA. The adaptive multilevel finite element solution of the Poisson-Boltzmann equation on massively parallel computers. IBM J Res Devel, 45, 427-38, 2001. http://dx.doi.org/10.1147/rd.453.0427

- APBS geometric flow solver
  - Chen Z, Baker NA, Wei GW. Differential geometry based solvation model I: Eulerian formulation, J Comput Phys, 229, 8231-58, 2010. http://dx.doi.org/10.1016/j.jcp.2010.06.036
  - Chen Z, Baker NA, Wei GW. Differential geometry based solvation model II: Lagrangian formulation. J Math Biol, 63, 1139-1200, 2011. http://dx.doi.org/10.1007/s00285-011-0402-z
  - Chen Z, Zhao S, Chun J, Thomas DG, Baker NA, Wei GW. Variational approach for nonpolar solvation analysis. Journal of Chemical Physics, 137, 084101, 2012. http://dx.doi.org/10.1063/1.4745084
  - Thomas DG, Chun J, Chen Z, Wei G, Baker NA. Parameterization of a Geometric Flow Implicit Solvation Model. Journal of Computational Chemistry, 34, 687-95, 2013. http://dx.doi.org/10.1002/jcc.23181
  - Daily M, Chun J, Heredia-Langner A, Baker NA. Origin of parameter degeneracy and molecular shape relationships in geometric-flow calculations of solvation free energies. J Chem Phys, 139, 204108, 2013. http://dx.doi.org/10.1063/1.4832900

- TABI-PB boundary element solver
  - Geng W, Krasny R. A treecode-accelerated boundary integral Poisson–Boltzmann solver for electrostatics of solvated biomolecules, J Comput Phys, 247, 62-78, 2013. https://doi.org/10.1016/j.jcp.2013.03.056

- Preparing protein structures and calculating pKa values
  - Dolinsky TJ, Nielsen JE, McCammon JA, Baker NA. PDB2PQR: an automated pipeline for the setup, execution, and analysis of Poisson-Boltzmann electrostatics calculations. Nucleic Acids Res, 32, W665-7, 2004. http://dx.doi.org/10.1093/nar/gkh381
  - Dolinsky TJ, Czodrowski P, Li H, Nielsen JE, Jensen JH, Klebe G, Baker NA. PDB2PQR: Expanding and upgrading automated preparation of biomolecular structures for molecular simulations. Nucleic Acids Res, 35, W522-5, 2007. http://dx.doi.org/10.1093/nar/gkm276
  - Carstensen T, Farrell D, Huang Y, Baker NA, Nielsen JE. On the development of protein pKa calculation algorithms. Proteins, 79, 3287-3298, 2011. http://dx.doi.org/10.1002/prot.23091
  - Alexov E, Mehler EL, Baker N, Baptista A, Huang Y, Milletti F, Nielsen JE, Farrell D, Carstensen T, Olsson MHM, Shen JK, Warwicker J, Williams, Word MJ. Progress in the prediction of pKa values in proteins. Proteins, 79, 3260-3275, 2011. http://dx.doi.org/10.1002/prot.23189
  - Gosink LJ, Hogan EA, Pulsipher TC, Baker NA. Bayesian model aggregation for ensemble-based estimates of protein pKa values. Proteins, 82 (3), 354-363, 2014. http://dx.doi.org/10.1002/prot.24390

- Structural bioinformatics based on electrostatic properties
  - Zhang X, Bajaj CL, Kwon B, Dolinsky TJ, Nielsen JE, Baker NA. Application of new multi-resolution methods for the comparison of biomolecular electrostatic properties in the absence of global structural similarity. Multiscale Model Simul, 5, 1196-213, 2006. http://dx.doi.org/10.1137/050647670
  - Chakraborty S, Rao BJ, Baker N, Ásgeirsson B. Structural phylogeny by profile extraction and multiple superimposition using electrostatic congruence as a discriminator. Intrinsically Disordered Proteins, 1 (1), e25463, 2013. https://www.landesbioscience.com/journals/idp/article/25463/

- Other fun with APBS and PDB2PQR

- Wagoner JA, Baker NA. Assessing implicit models for nonpolar mean solvation forces: the importance of dispersion and volume terms. Proc Natl Acad Sci USA, 103, 8331-6, 2006. http://dx.doi.org/10.1073/pnas.0600118103
- Swanson JMJ, Wagoner JA, Baker NA, McCammon JA. Optimizing the Poisson dielectric boundary with explicit solvent forces and energies: lessons learned with atom-centered dielectric functions. J Chem Theory Comput, 3, 170-83, 2007. http://dx.doi.org/10.1021/ct600216k
- Schnieders MJ, Baker NA, Ren P, Ponder JW. Polarizable Atomic Multipole Solutes in a Poisson-Boltzmann Continuum. J Chem Phys, 126, 124114, 2007. http://dx.doi.org/10.1063/1.2714528
- Callenberg KM, Choudhary OP, de Forest GL, Gohara DW, Baker NA, Grabe M. APBSmem: A graphical interface for electrostatic calculations at the membrane. PLoS ONE, 5, e12722, 2010. http://dx.doi.org/10.1371/journal.pone.0012722
- Unni S, Huang Y, Hanson RM, Tobias M, Krishnan S, Li WW, Nielsen JE, Baker NA. Web servers and services for electrostatics calculations with APBS and PDB2PQR. J Comput Chem, 32 (7), 1488-1491, 2011. http://dx.doi.org/10.1002/jcc.21720
- Konecny R, Baker NA, McCammon JA. iAPBS: a programming interface to the adaptive Poisson–Boltzmann solver. Computational Science and Discovery, 5, 015005, 2012. http://dx.doi.org/10.1088/1749-4699/5/1/015005

CHAPTER 13

Documentation TODO list

Todo

Under construction; please see https://arxiv.org/abs/1705.10035 for an initial discussion. Saved as issue https://github.com/Electrostatics/apbs-pdb2pqr/issues/481

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/errors.rst, line 62.)

Todo

Resolve unit confusion with geometric flow *gamma* keyword. https://github.com/Electrostatics/apbs-pdb2pqr/issues/490

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/apolar/gamma.rst, line 15.)

Todo

Resolve unit confusion with geometric flow `press` keyword and the apolar *press* keyword. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/499

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/apolar/press.rst, line 16.)

Todo

The PB-(S)AM `3dmap` keyword should not exist; please replace it ASAP with the *write* command. Documented this todo as https://github.com/Electrostatics/apbs-pdb2pqr/issues/482

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/3dmap.rst, line 14.)

Todo

What are the units for `dRot`? Documented as https://github.com/Electrostatics/apbs-pdb2pqr/issues/486

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/diff.rst, line 32.)

Todo

Add a `mol id` flag rather than have an implicit ordering of the `diff` keywords. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/487

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/diff.rst, line 41.)

Todo

The PB-(S)AM `dx` keyword should not exist; please replace it ASAP with the *write* command. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/488

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/dx.rst, line 14.)

Todo

It would be better to generalize the *READ input file section* section of the input file rather than use the `exp` command. This command also needs to be cleaned up – it's too fragile. Documented at https://github.com/Electrostatics/apbs-pdb2pqr/issues/489

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/exp.rst, line 17.)

Todo

Resolve unit confusion with geometric flow *gamma* keyword. https://github.com/Electrostatics/apbs-pdb2pqr/issues/490

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/gamma-geoflow.rst, line 17.)

Todo

Add LPBE/NPBE support to geometric flow or remove the `ion` and `lpbe` keywords. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/491

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/geoflow-auto.rst, line 43.)

Todo

If there's only one mode, then we can change the keyword from `geoflow-auto` to just `geoflow`. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/492

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/geoflow-auto.rst, line 48.)

Todo

The PB-(S)AM `grid2d` keyword should not exist; please replace it ASAP with the *write* command. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/493

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/grid2d.rst, line 25.)

Todo

The PB-(S)AM `gridpts` keyword should not exist; it's duplicative of the existing *dime* keyword! Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/494

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/gridpts.rst, line 14.)

Todo

It would be better to generalize the *READ input file section* section of the input file rather than use the `imat` command. This command also needs to be cleaned up – it's too fragile. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/495

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/imat.rst, line 16.)

Todo

The integer flag values for `mesh` should be replaced by human-readable strings. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/496

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/mesh.rst, line 28.)

Todo

The `msms` keyword should be removed and replaced with a more general alternative: either the *mesh* surface option in *tabi* or the existing APBS *srfm (elec)*. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/497

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/msms.rst, line 11.)

Todo

The integer flag values for `mesh` should really be replaced by human-readable strings.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/outdata.rst, line 22.)

Todo

If there's only one mode to PBAM, let's call it `pbam` instead of `pbam-auto`. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/498

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/pbam-auto.rst, line 11.)

Todo

If there's only one mode to PBAM, let's call it `pbsam` instead of `pbsam-auto`.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/pbsam-auto.rst, line 11.)

Todo

Resolve unit confusion with geometric flow `press` keyword and the apolar *press* keyword. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/499

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/press-geoflow.rst, line 18.)

Todo

The dynamics part of the PB-(S)AM code should be moved out of the `ELEC` section. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/500

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/runtype.rst, line 37.)

Todo

The PB-(S)AM `salt` keyword should be eradicated and replaced with the *ion* keyword. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/501

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/salt.rst, line 14.)

Todo

The PB-SAM `surf` command is redundant with and should be replaced by the existing *usemesh* command. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/502

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/surf.rst, line 15.)

Todo

Add a constant keyword (e.g., like `position`) before the `{pos}` argument of `term`. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/503

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/term.rst, line 33.)

Todo

We need documentation for `tolsp`. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/504

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/tolsp.rst, line 9.)

Todo

It would be great to use the same units everywhere in APBS. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/485

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/units.rst, line 25.)

Todo

It would be nice to incorporate the `xyz` functionality into the *READ input file section* block. Documented in https://github.com/Electrostatics/apbs-pdb2pqr/issues/505

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/input/elec/xyz.rst, line 20.)

Todo

Move Programmer's Guide to Sphinx.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/apbs/programming.rst, line 6.)

Todo

Link binding energy examples directly from the source tree.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/examples/binding-energies.rst, line 74.)

Todo

Migrate geoflow, pbsam, pbam examples over from `examples` directory.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/examples/index.rst, line 41.)

Todo

Add VMD tutorial.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/examples/index.rst, line 67.)

Todo

Migrate PDB2PQR XML format information over from programmer's guide.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/formats/index.rst, line 51.)

Todo

Provide documentation of the PDB2PQR DAT and NAMES formats.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/pdb2pqr/extending.rst, line 30.)

Todo

Incorporate PDB2PQR Python documentation into Sphinx rather than entering it here manually.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/pdb2pqr/extending.rst, line 175.)

Todo

Make sure user extensions are adequately documented.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/pdb2pqr/invoking.rst, line 12.)

Todo

Replace this section with automagically generated documentation ala https://sphinx-argparse.readthedocs.io/en/stable/

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/pdb2pqr/invoking.rst, line 29.)

Todo

Make sure that PDB2PQR force fields are referenced and described.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/pdb2pqr/invoking.rst, line 96.)

Todo

Enable Google Analytics support.

(The original entry is located in /home/docs/checkouts/readthedocs.org/user_builds/apbs-pdb2pqr/checkouts/latest/doc/todo.rst, line 7.)

Todo

Enable Google Analytics support.

Bibliography

[Azuara2006] Azuara C, Lindahl E, Koehl P, Orland H, and Delarue M, PDB_Hydro: incorporating dipolar solvents with variable density in the Poisson-Boltzmann treatment of macromolecule electrostatics. Nucleic Acids Research, 2006. 34: p. W38-W42.

[Baker2005] Baker NA, Biomolecular Applications of Poisson-Boltzmann Methods, in Reviews in Computational Chemistry, Lipkowitz KB, Larter R, and Cundari TR, Editors. 2005, John Wiley and Sons.

[Chen2010] Chen Z, Baker NA, Wei GW. Differential geometry based solvation model I: Eulerian formulation, J Comput Phys, 229, 8231-58, 2010.

[Chu2007] Chu VB, Bai Y, Lipfert J, Herschlag D, and Doniach S, Evaluation of Ion Binding to DNA Duplexes Using a Size-Modified Poisson-Boltzmann Theory. Biophysical Journal, 2007. 93(9): p. 3202-9.

[Fogolari2002] Fogolari F, Brigo A, and Molinari H, The Poisson-Boltzmann equation for biomolecular electrostatics: a tool for structural biology. Journal of Molecular Recognition, 2002. 15(6): p. 377-92.

[Grochowski2007] Grochowski P, lstrok A, and Trylska J, Continuum molecular electrostatics, salt effects and counterion binding. A review of the Poisson-Boltzmann theory and its modifications. Biopolymers, 2007. 89(2): p. 93-113.

[Lamm2003] Lamm G, The Poisson-Boltzmann Equation, in Reviews in Computational Chemistry, Lipkowitz KB, Larter R, and Cundari TR, Editors. 2003, John Wiley and Sons, Inc. p. 147-366.

[Levy2003] Levy RM, Zhang LY, Gallicchio E, and Felts AK, On the nonpolar hydration free energy of proteins: surface area and continuum solvent models for the solute-solvent interaction energy. Journal of the American Chemical Society, 2003. 125(31): p. 9523-30.

[Netz2000] Netz RR and Orland H, Beyond Poisson-Boltzmann: Fluctuation effects and correlation functions. European Physical Journal E, 2000. 1(2-3): p. 203-14.

[Ren2012] Ren P, Chun J, Thomas DG, Schnieders M, Marucho M, Zhang J, Baker NA, Biomolecular electrostatics and solvation: a computational perspective. Quarterly Reviews of Biophysics, 2012. 45(4): p. 427-491.

[Roux1999] Roux B and Simonson T, Implicit solvent models. Biophysical Chemistry, 1999. 78(1-2): p. 1-20.

[Vitalis2004] Vitalis A, Baker NA, McCammon JA, ISIM: A program for grand canonical Monte Carlo simulations of the ionic environment of biomolecules, Molecular Simulation, 2004, 30(1), 45-61.

[Wagoner2006] Wagoner JA and Baker NA, Assessing implicit models for nonpolar mean solvation forces: the importance of dispersion and volume terms. Proceedings of the National Academy of Sciences of the United States of America, 2006. 103(22): p. 8331-6.

[Warshel2006] Warshel A, Sharma PK, Kato M, and Parson WW, Modeling electrostatic effects in proteins. Biochimica et Biophysica Acta (BBA) - Proteins & Proteomics, 2006. 1764(11): p. 1647-76.

Python Module Index

Index