

CHARMM Element doc/scpism.doc \$Revision: 1.1 \$

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Screened Coulomb Potentials Implicit Solvent Model (SCPISM)

The SCPISM is a continuum model of solvated macromolecules that treats implicitly the effects of the surrounding aqueous medium. The model is based on screened Coulomb potentials (SCP) as derived from theory of polar liquids (the Lorentz-Debye-Sack theory). At the present level of development the model only incorporates a continuum description of electrostatic effects and, optionally, a simple term accounting for hydrophobic interactions.

The current implementation is suitable for molecular dynamics simulations, energy evaluation and minimization of peptides and proteins.

An overview of the physical ideas that led to the development of the model can be found in <http://cmm.cit.nih.gov/~mago/> (for details see refs. below). The present version of the program will be revised and upgraded in the future. In particular the parameterization is still under development. The parameters used in all applications of the SCPISM reported to date have not been corrected or adjusted since the model was first introduced (actually, this is a long-term desirable feature of the SCPISM as discussed in [1-4], although corrections of the present parameters are probably needed, especially those governing HB interactions). There is one parameter per atom type. The original parameterization was done based on solvation energies of amino acid side chain analogs and restrictions imposed to the space of parameters, as reported [2] (the parameterization was not based on reproducing PB results, only experimental data). Hydrogen bonding strength is treated independently (this was shown to be essential for structure prediction and stabilization as discussed in the refs.). The refinement of HB interactions, along with the introduction of solvent exclusion effects and the effect of salt, are currently in development and will appear in future versions of the model. In particular HB are currently being calibrated based on results of PMF between all possible interactions in amino acids, calculated using extensive MD simulations in explicit solvent (S A Hassan, submitted).

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SCPISM commands

An effort was made to minimize the number of input options available to the user (i.e., no parameters are allowed to be modified from outside; the physics of the system is already incorporated into

the model and, then, hard-wired into the code). To activate the model the following command line is used:

```
SCPIsm [UIsm int] (1)
```

where UIsm is the unit number for reading the SCP parameters. These parameters are stored in scpism.inp and must be opened for reading in the usual way before the model is requested (see example below), i.e.,

```
OPEN READ UNIT int CARD NAME "scpism.inp"
```

Once the model is requested, any options for energy, minimization and dynamics calculations are supported. Note, however, that the 'interaction energy' is not a simple concept in the SCPISM because of the self-energy terms, so care should be exercised when the INTER command of CHARMM is used.

Electrostatics interactions are truncated using a standard shift function (any other specification of cutoff of electrostatics is automatically disabled once the SCPISM is requested; although other options could be incorporated, it can be shown that this cutoff scheme is appropriate within the SCPISM because of the nonlinearity of the screening function).

The code has not yet been parallelized, so only the serial version is available.

Any restraining option that is introduced as an additional term in the potential is supported; use of the CONS FIX constraints are not recommended because they are inconsistent with the way the self-energies are calculated: the calculation of Born radii in the SCPISM requires the positions of all the atoms around each atom of the system to be available (in particular the positions of the fixed atoms) because it is based on a contact model approach; therefore, it is advised not to use this CHARMM feature when the SCPISM is on. It is possible (but not required) to deactivate the model once any of the required tasks (energy evaluation, minimization or dynamics) is completed. To exit the model use

```
SCPIsm END
```

in this case CHARMM will return to the default electrostatics options (the model can be switched on again at any point later in the input file).

Note that, although the current implementation of the SCPISM describes only electrostatic effects, to be consistent with earlier applications of the model, an overall hydrophobic term proportional to the total solvent accessible surface area (SASA), also based on a contact model approach, can be requested by using the subcommand HYDRophobic in the command line (1) above. If this term is not activated, other model accounting for hydrophobic interactions must be used.

The CPU time of the SCPISM is shown to be between 2 and 3 times slower than the same calculation in vacuum (depending on the platform and optimization of compilation). This performance was evaluated in 4000 steps of energy minimization of Protein G, using ABNR and several cutoff distances between 12.0 and 20 Angs.

Monte Carlo simulations is not advised with this initial implementation of the model because the hydrogen bonding (HB) algorithm has been simplified for MD simulations (see [2,3]). Extension of the model for MC is currently under way.

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Structure of the parameter input file:

All the parameters required for the model are atom-type based and are collected in a single file. Determination of these parameters was described in Refs. [2,3]. The parameters have been optimized in the context of the PAR22 all-atom force field.

SCPISM parameter file has the following format (note that not all fields in this file are parameters that controls the electrostatics):

H	0.4906	0.6259	0.5000	0.7004	0.3700	0.0052	PH ! polar H
HC	0.5300	9.6746	0.5000	0.7280	0.3700	0.0052	PH ! N-ter H
HA	0.5300	0.5000	0.5000	0.7280	0.3700	0.0052	! nonpolar H
HT	0.4906	2.3800	0.5000	0.7004	0.3700	0.0052	PH ! TIPS3P WATER HYDROGEN
HP	0.5274	0.5000	0.5000	0.7262	0.3700	0.0052	! aromatic H
HB	0.4858	0.5000	0.5000	0.6970	0.3700	0.0052	! backbone H
HR1	0.4651	0.5000	0.5000	0.6820	0.3700	0.0052	! his hel, (+)his HG,HD2
HR2	0.4580	0.5000	0.5000	0.6768	0.3700	0.0052	! (+) his HE1

Col. 1: Atom type defined in PAR22

Col. 2: α_i controls slope of $D(r)$ around atom-type i

Col. 3: for PH interaction with PA this value controls the Born radius of PH to modulate hydrogen bonding strength (see URL); the increase or decrease of the PH Born radius is defined by the product $\text{Col.3(PH)} \times \text{Col.3(PA)}$ As a rule, the larger the value of this product, the weaker the HB interaction.

Col. 4: Extension of Born radius R_{iw} to obtain R_{ip} , i.e., $R_{ip} = R_{iw} + \text{Col.4}$ (see [1]); only one value for atoms considered

Col. 5: $\text{SQRT}(\alpha_i)$; this is needed for $\alpha_{ij} = \alpha_i \alpha_j$ (see [1,2])

Col. 6: covalent radius for each atom (only 5 values considered, i.e., for C,N,O,S,H)

Col. 7: γ_i in hydrophobic energy = sum over i of $\gamma_i \text{SASA}_i$ (note that all coefficients are equal in this first release)

Col. 8: denotes atoms involved in H-bonding (PH = polar proton; PA = proton acceptor)

Theoretical background of the SCPISM

The SCPISM is based on screening functions $D(r)$ that modulate the electric potential $\phi(r)$ in the system, rather than the dielectric functions $\epsilon(r)$ that modulates the electric field $E(r)$. The relation between both functions is obtained from the definition $E(r) = -\text{Grad}[\phi(r)]$

See URL above for details.

Because of the relationship between $D(r)$ and $\epsilon(r)$, both functions are sigmoidal with r . Once $\epsilon(r)$ is known from theory or experiments, the screening function that characterizes the medium is obtained by

numerical integration. Based on these results, the SCPISM uses atom type-dependent sigmoidal functions in the context of the all-atom representation PAR22.

In the SCPISM the standard electrostatic component of the force field is replaced by terms that describe both the electrostatic interaction energy, and the self energy. The screening functions are continuous functions of the position and describes a dielectric medium that permeates all of space. For the solvated protein, $D(r)$ approaches bulk medium value of the screening only far from the protein (see [4] for a discussion). Therefore, the SCPISM does not introduce either an internal or an external dielectric constant, and therefore, there is no boundary that separates the protein from the solvent (see URL). In contrast with other implicit models, e.g., in GB models, the SCPISM is formally derived under basic physical theory of polar solvation; the model is being constructed step by step to incorporate all the physical effects that are removed when the explicit solvent is eliminated (see URL for a discussion on this topic).

Because the effective screening functions that characterize the overall modulation of the electrostatics are obtained from properties of bulk solvent, short-range interactions characterizing hydrogen bonding (HB) must be corrected (see [3] and URL). This is also needed to incorporate the effect of explicit competition with water molecules (S A Hassan, submitted). To obtain a reasonable representation of HB strength in solvent medium, all individual HB interactions available in proteins are individually calibrated via the self-energy terms (based on experimentally estimated values (see Refs.[2,3]; currently this is being reviewed and HB strength is adjusted based on PMF calculation in explicit solvent as described above). The stabilization of HB energies is carried out based on charge states of the interacting groups, as well as on hybridization states of proton donor and acceptor atoms [3]. For the current implementation suitable for MD simulations this approach was simplified with respect to the original development for MC simulations, and in this first implementation the HB interactions depend only on atom type (H and HC interacting with O, OC, OH1 and NR2) and no directionality has been included.

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References

below are the main references for the current implementation into charmm. More comprehensive bibliography is available in the URL.

- [1] S A Hassan, E L Mehler, D Zhang and H Weinstein, Molecular Dynamics Simulations of Peptides and Proteins with a Continuum Electrostatic Model based on Screened Coulomb Potentials; Proteins 51, 109 (2003)
- [2] S A Hassan, F Guarnieri and E L Mehler, A General Treatment of Solvent Effects based on Screened Coulomb Potentials; J Phys Chem B 104, 6478 (2000)
- [3] S A Hassan, F Guarnieri and E L Mehler, Characterization of Hydrogen Bonding in a Continuum Solvent Model; J Phys Chem B 104, 6490 (2000)

[4] S A Hassan and E L Mehler, Critical Analysis of Continuum Electrostatics: the Screened Coulomb Potential Implicit Solvent Model and the Study of the Alanine Dipeptide and Discrimination of Misfolded Structures of Proteins; Proteins 47, 45 (2002)

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SCPISM example input file

```
-----  
* energy, minimization and dynamics with the SCPISM  
*  
  
open read card unit 10 name top22.inp  
read rtf unit 10 card  
close unit 10  
  
open read card unit 10 name par22.inp  
read para unit 10 card  
close unit 10  
  
open read unit 10 card name SCPISM.inp  
  
! define system  
generate main setup  
  
open read unit 2 card name filename.crd  
read coor card unit 2  
close unit 2  
  
! set up all options for the run (nbond cutoff distance, shake, vdW, etc)  
! these options can also be specified in the 'energy' command line, as usual  
  
! request SCPISM  
  
SCPI HYDR UISM 10  
  
! this will activate electrostatics and a simple hydrophobic term;  
! if other model is used to describe hydrophobic interactions then  
! replace the above command line by: SCPI UISM 3  
  
! now calculate energy, minimize structure and run dynamics  
  
ener  
  
mini [options]  
  
dyna [options]  
  
! exit SCPISM  
  
SCPI END  
  
! if needed, the model can be requested again at any point
```

stop
