

Table 7.2 Overview of Currently Used Scoring Functions

Type of Function	Name of Function	Year Published	Original References	Selected References to Applications
Force field	Charmm	1998	(274)	
Force field + desolvation	(Schapira, Abagyan et al.)	1999	(280)	
	AMBER + desolvation	1999	(276)	
	Charmm + PB	1999	(393)	
	AMBER + desolvation	1999	(278)	
	MM PB/SA	1999	(343)	(344, 346)
Linear response	LIE	1994	(260)	(261, 263, 394)
Simplified free-energy perturbation	OWFEG Grid	2001	(284)	(395)
Empirical	(Wade, Goodford et al.) SCORE1	1989, 1993 1994	(220, 298) (294)	GRID (218) LUDI (108, 109); (300, 396)
	(Miller, Sheridan et al.) GOLD score	1994 1995	(121) (176, 177)	FLOG (121) GOLD (176, 177)
	PLP	1995, 2000	(185, 367)	
	FlexX score	1996	(110)	FlexX (110, 130, 138, 397)
	VALIDATE	1996	(307)	
	(Jain)	1996	(297)	Hammerhead (388)
	ChemScore	1997	(80)	(295)
	SCORE2	1998	(296)	
	(Takamatsu, Itai)	1998	(398)	
	SCORE	1998	(293)	(225)
	AutoDock3	1998	(115)	(391)
	Fresno	1999	(399)	(230)
	ScreenScore	2001	(287)	
Desolvation terms	HINT	1991	(400)	(308)
	(Zhang, DeLisi et al.)	1997	(305)	
Knowledge-based	SMoG	1996	(313)	SMoG (314)
	BLEEP	1999	(315, 316)	(340)
	PMF	1999	(317)	(299, 319, 320, 339, 369)
	DrugScore	2000	(226)	(15, 318)

ing affinity. In doing so, one substitutes estimates of the free energy of binding in solution by an estimate of the gas phase enthalpy of binding. Even this crude approximation can lead to satisfying results. A good correlation was obtained between nonbonded interaction energies calculated with a modified MM2 force field and  $IC_{50}$  values of 33 HIV-1 protease inhibitors (269). Similar results were reported in a study of 32 thrombin-inhibitor complexes with the CHARMM force field (270). In both

studies, however, experimental data represented rather narrow activity ranges and covered little structural variation.

The AMBER (271, 272) and CHARMM (179) nonbonded terms are used as scoring function in several docking programs. As mentioned above (Section 3.1.1), protein terms are usually precalculated on a rectangular grid to speed up the energy calculation compared to traditional atom-by-atom evaluations (273). Distance-dependent dielectric constants are