Supporting Information

Validation of Molecular Docking Programs for

Virtual Screening against Dihydropteroate Synthase

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Table 1S. DOCK Docking of the ACD Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	Grid Score	F-Score	PMF-Score	G-Score	D-Score	ChemScore
Grid Score	---	.748	.155	<.001	<.001	<.001
F-Score	.237	---	.298	.016	.551	.004
PMF-Score	.975	.154	---	<.001	.006	<.001
G-Score	<.001	.002	<.001	---	.004	.764
D-Score	<.001	.024	<.001	.008	---	.041
ChemScore	.001	.003	<.001	.265	.043	---

Table 2S. DOCK Docking of the Schrödinger Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	Grid Score	F-Score	PMF-Score	G-Score	D-Score	ChemScore
Grid Score	---	.762	.003	.002	.003	.007
F-Score	.161	---	.125	.005	.333	<.001
PMF-Score	<.001	.774	---	<.001	<.001	<.001
G-Score	.008	.002	<.001	---	.076	.422
D-Score	.056	.053	<.001	.267	---	.085
ChemScore	.047	<.001	<.001	.467	.165	---

Table 3S. DOCK Docking of the ZINC Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	Grid Score	F-Score	PMF-Score	G-Score	D-Score	ChemScore
Grid Score	---	.862	.030	<.001	.002	.001
F-Score	.310	---	.119	.002	.515	.001
PMF-Score	<.001	.665	---	<.001	.001	<.001
G-Score	<.001	.002	<.001	---	.005	.924
D-Score	<.001	.077	<.001	.005	---	.074
ChemScore	.008	.001	<.001	.911	.162	---

Table 4S. FlexX Docking of the ACD Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	F-Score	PMF-Score	G-Score	D-Score	ChemScore
F-Score	---	.537	<.001	.019	<.001
PMF-Score	.485	---	<.001	.003	<.001
G-Score	.002	<.001	---	.005	.918
D-Score	.017	<.001	.001	---	.010
ChemScore	<.001	<.001	.331	.033	---

Table 5S. FlexX Docking of the Schrödinger Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	F-Score	PMF-Score	G-Score	D-Score	ChemScore
F-Score	---	.032	<.001	.011	<.001
PMF-Score	.076	---	<.001	<.001	<.001
G-Score	.021	<.001	---	.023	.324
D-Score	.030	<.001	.049	---	.001
ChemScore	<.001	<.001	.184	.028	---

Table 6S. FlexX Docking of the ZINC Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	F-Score	PMF-Score	G-Score	D-Score	ChemScore
F-Score	---	.052	<.001	.017	<.001
PMF-Score	.051	---	<.001	<.001	<.001
G-Score	.010	<.001	---	.006	.471
D-Score	.042	<.001	.013	---	.001
ChemScore	<.001	<.001	.224	.028	---

Table 7S. Glide Docking of the ACD Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	Glide Score	F-Score	PMF-Score	G-Score	D-Score	ChemScore
Glide Score	---	.909	.054	<.001	<.001	<.001
F-Score	.985	---	.027	<.001	<.001	<.001
PMF-Score	.142	.317	---	<.001	<.001	<.001
G-Score	<.001	<.001	<.001	---	.022	<.001
D-Score	<.001	<.001	<.001	.031	---	.870
ChemScore	.003	<.001	.002	<.001	.981	---

Table 8S. Glide Docking of the Schrödinger Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	Glide Score	F-Score	PMF-Score	G-Score	D-Score	ChemScore
Glide Score	---	.124	.021	<.001	<.001	<.001
F-Score	.371	---	.140	<.001	<.001	<.001
PMF-Score	.089	.529	---	<.001	<.001	<.001
G-Score	<.001	<.001	<.001	---	.338	.236
D-Score	<.001	<.001	<.001	.342	---	.966
ChemScore	<.001	<.001	.005	.625	.811	---

Table 9S. GOLD Docking of the ZINC Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	GOLD Score	F-Score	PMF-Score	G-Score	D-Score	ChemScore
GOLD Score	---	.077	.029	<.001	<.001	<.001
F-Score	.005	---	.863	<.001	<.001	<.001
PMF-Score	.007	.708	---	<.001	<.001	<.001
G-Score	<.001	.002	<.001	---	.958	.024
D-Score	<.001	.002	<.001	.639	---	.010
ChemScore	<.001	<.001	<.001	.221	.012	---

Table 10S. Surflex Docking of the ACD Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	Surflex Score	F-Score	PMF-Score	G-Score	D-Score	ChemScore
Surflex Score	---	.963	.002	<.001	<.001	<.001
F-Score	.460	---	.008	<.001	<.001	<.001
PMF-Score	.003	<.001	---	<.001	<.001	<.001
G-Score	<.001	<.001	<.001	---	.001	<.001
D-Score	<.001	<.001	<.001		---	.460
ChemScore	<.001	<.001	<.001	<.001	.447	---

Table 11S. Surflex Docking of the ZINC Decoy Set. Comparison of p values for AU-ROC's (yellow) and SSLR statistics (green) for each scoring function.

Docking Program / Validation Set	Surflex Score	F-Score	PMF-Score	G-Score	D-Score	ChemScore
Surflex Score	---	.499	.172	<.001	<.001	<.001
F-Score	.475	---	.327	<.001	<.001	<.001
PMF-Score	.194	.472	---	<.001	<.001	<.001
G-Score	<.001	<.001	<.001	---	.006	<.001
D-Score	<.001	<.001	<.001	.021	---	.249
ChemScore	<.001	<.001	<.001	<.001	.258	---

Figure 1S. DOCK - ACD Decoy Set, ROC Curves
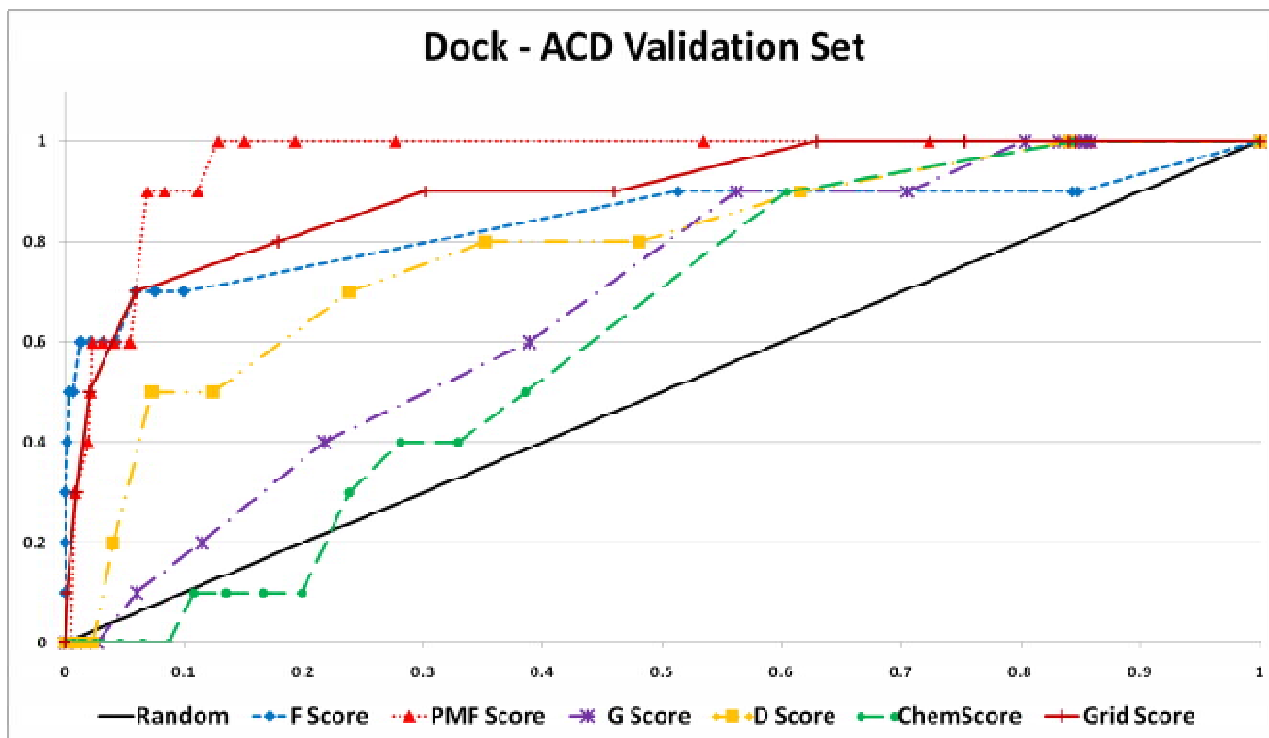
Figure 2S. DOCK - Schrodinger Decoy Set, ROC Curves
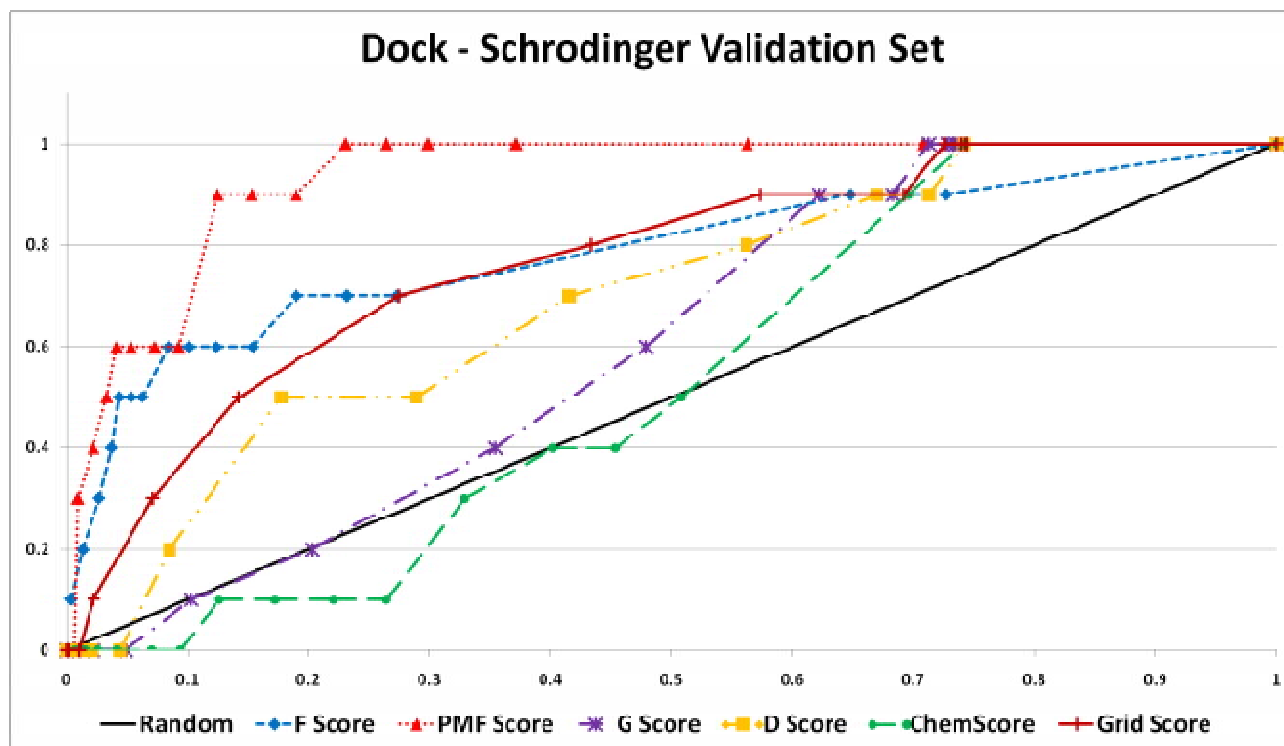

Dock - Schrodinger Validation Set

Figure 3S. DOCK - ZINC Decoy Set, ROC Curves
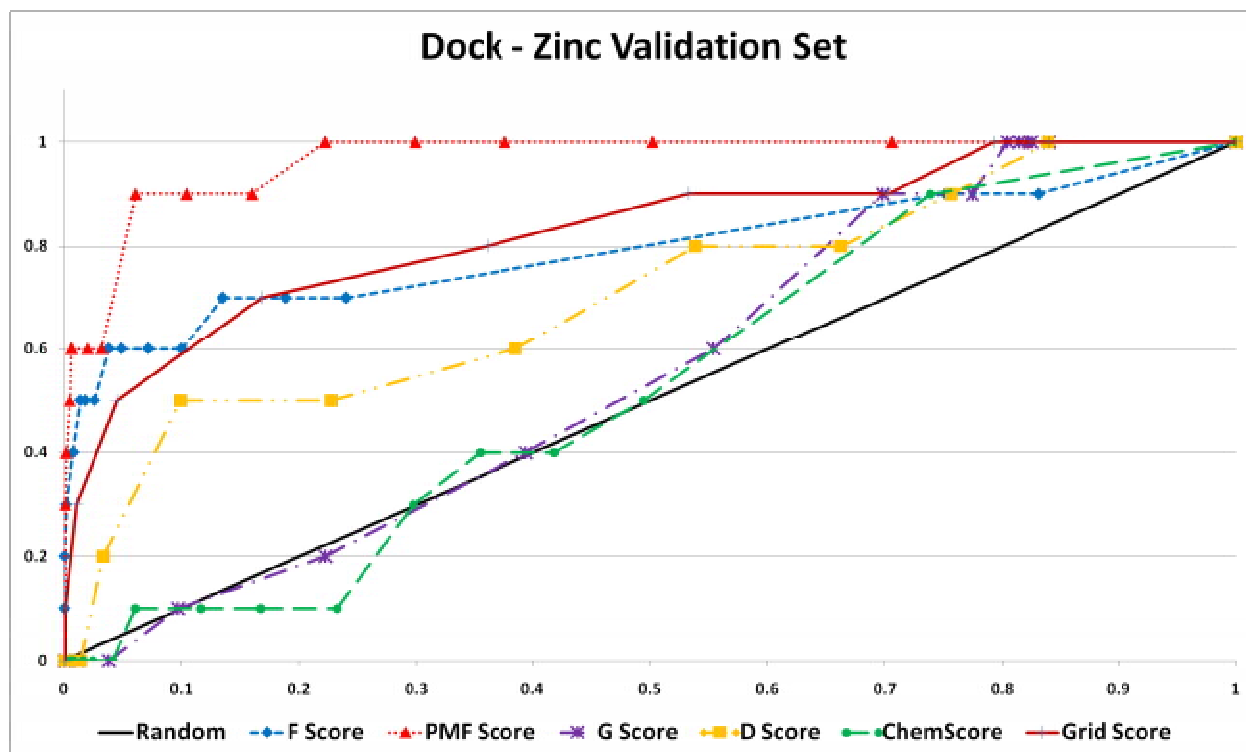
Figure 4S. FlexX - ACD Decoy Set, ROC Curves
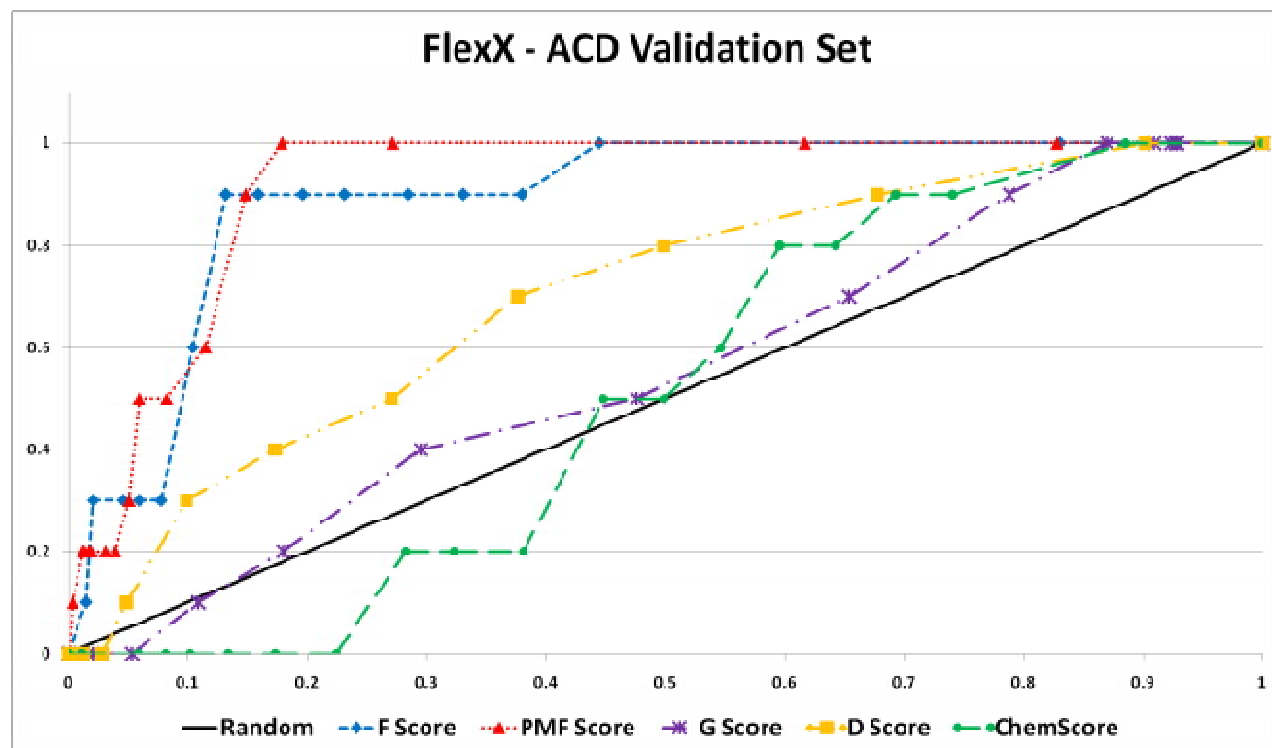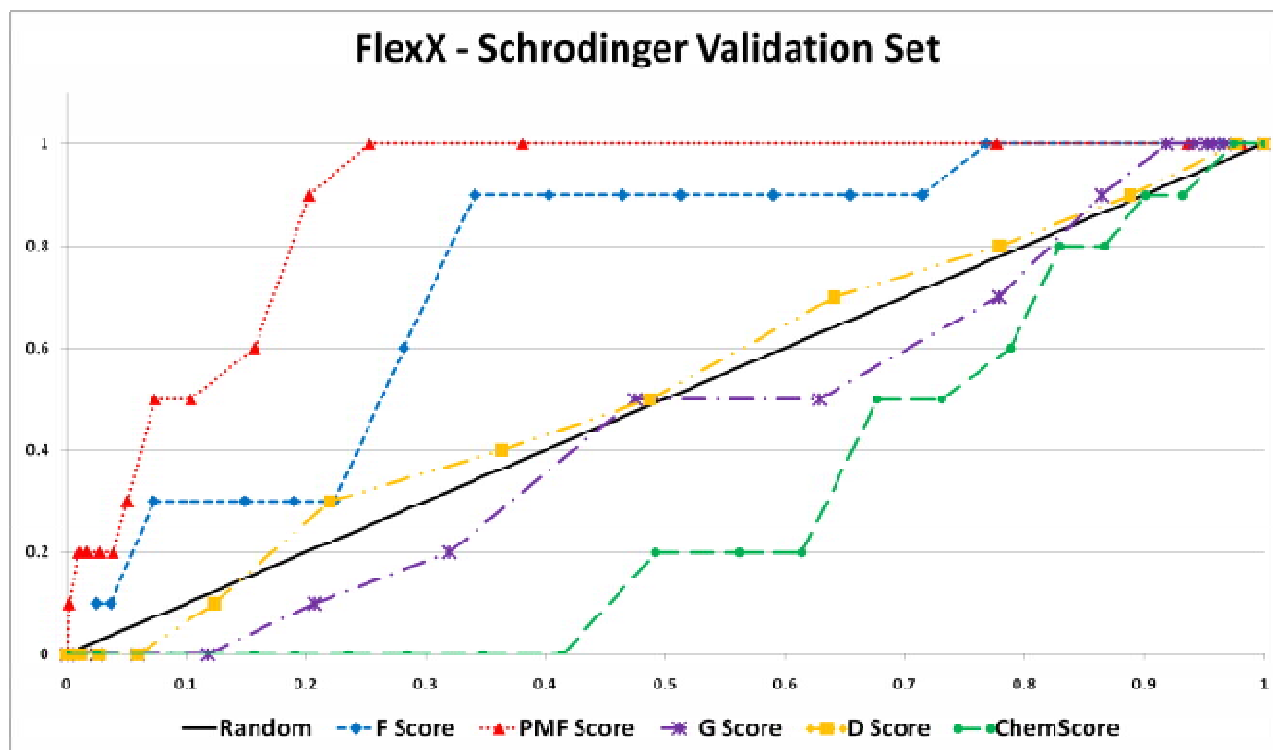
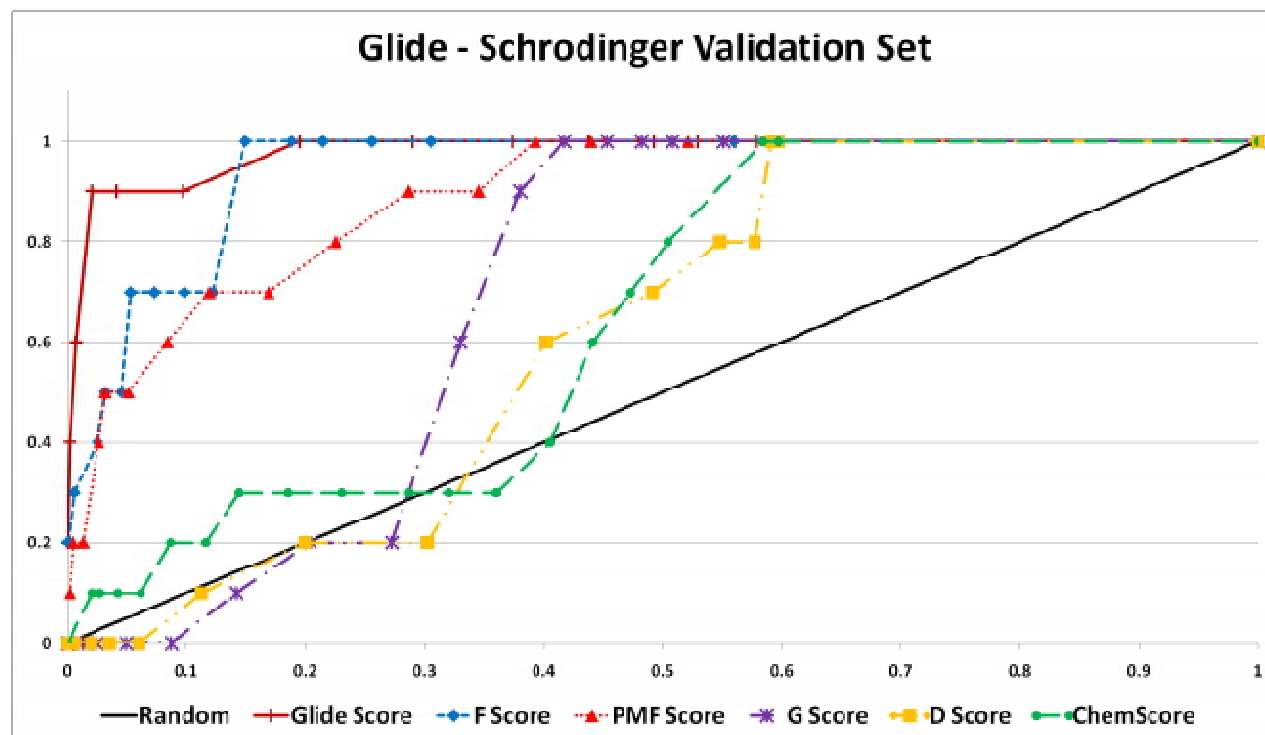**Figure 5S. FlexX - Schrodinger Decoy Set, ROC Curves**

FlexX - Schrodinger Validation Set

— Random — F Score — PMF Score — G Score — D Score — ChemScore

Figure 6S. FlexX - ZINC Decoy Set, ROC Curves
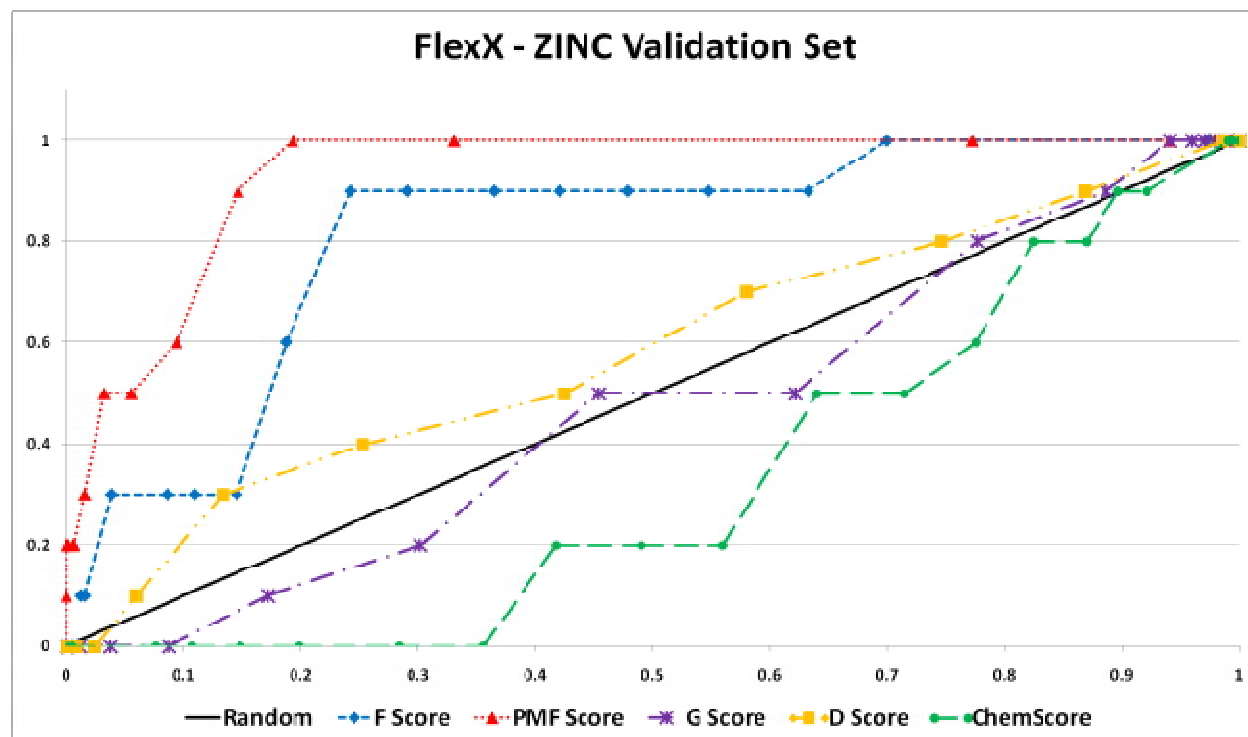
Figure 7S. Glide - ACD Decoy Set, ROC Curves

Glide - ACD Validation Set
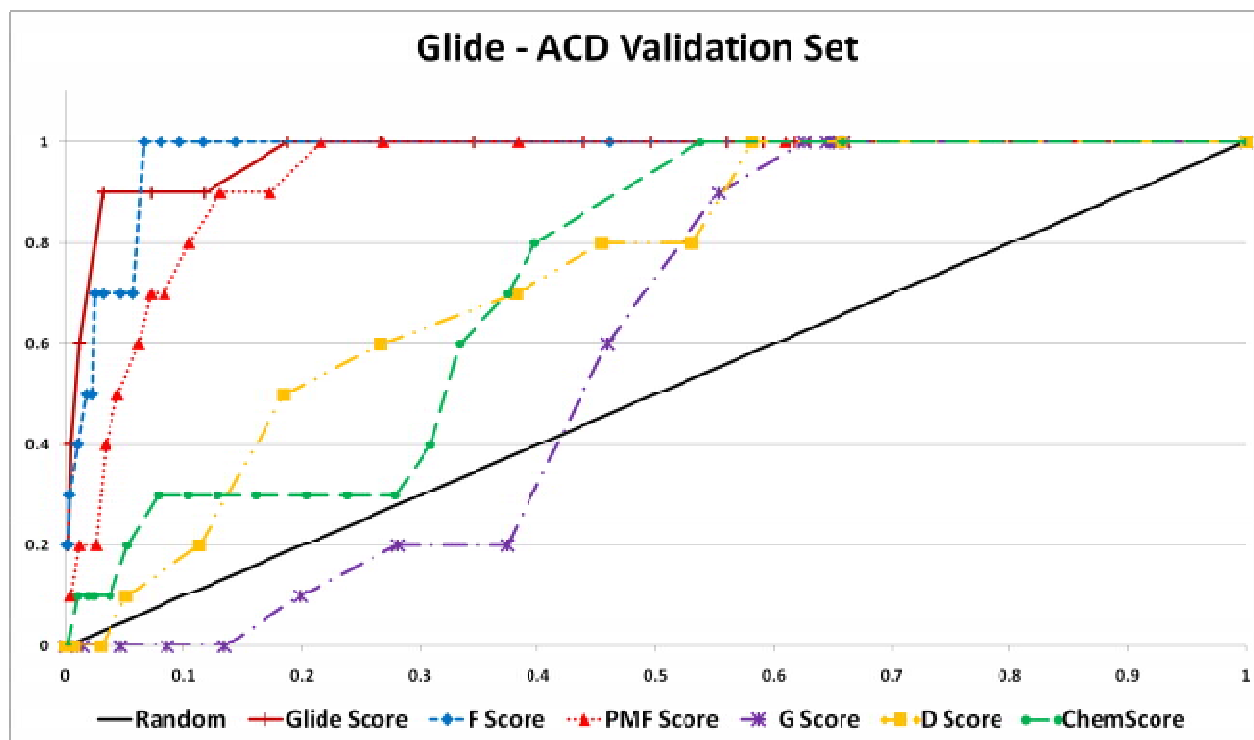
Figure 8S. Glide - Schrodinger Decoy Set, ROC Curves

Glide - Schrodinger Validation Set

Figure 9S. Gold - ZINC Decoy Set, ROC Curves

Gold - Zinc Validation Set

Legend: Random, Gold Score, F Score, PMF Score, G Score, D Score, ChemScore
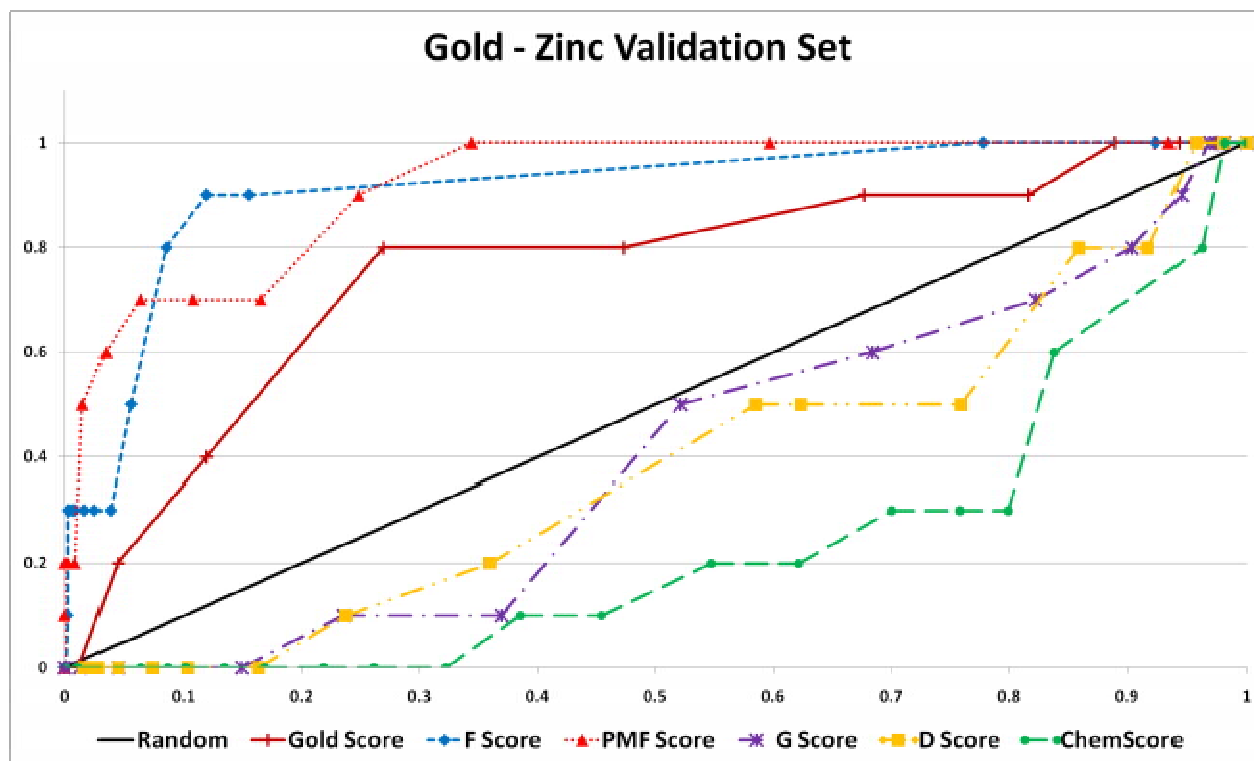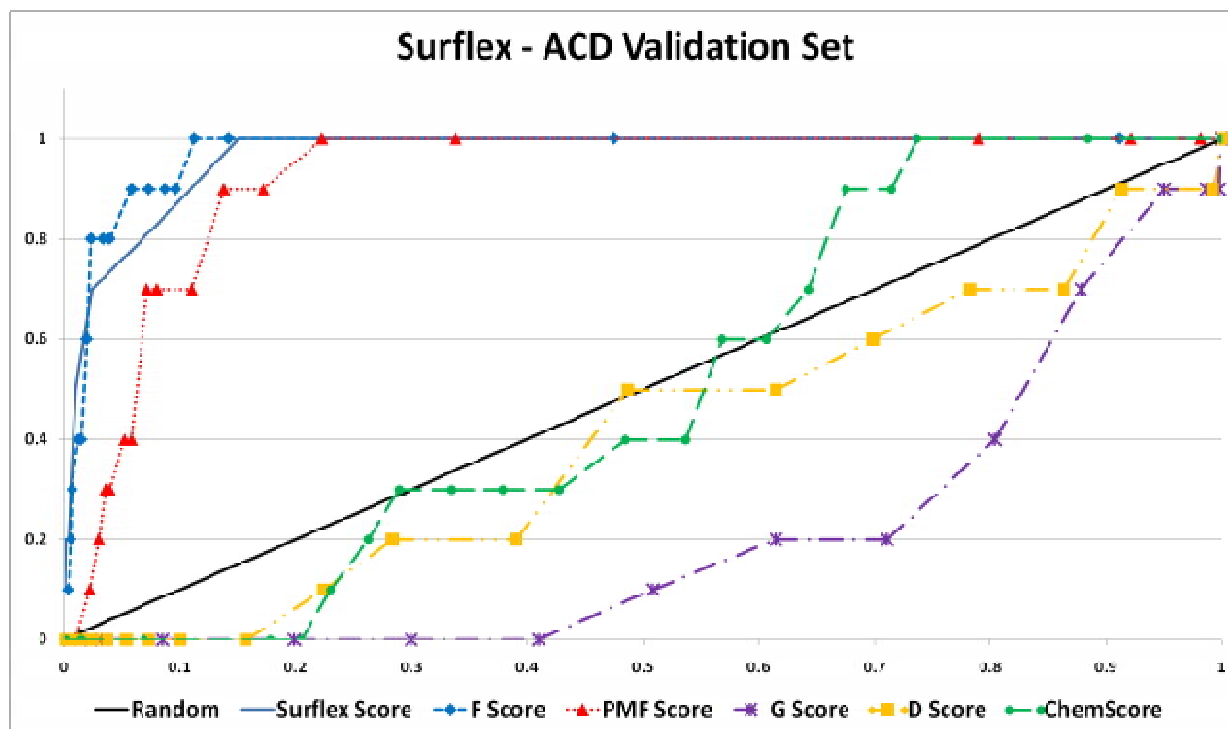
Figure 10S. Surflex - ACD Decoy Set, ROC Curves

Figure 11S. Surflex - ZINC Decoy Set, ROC Curves
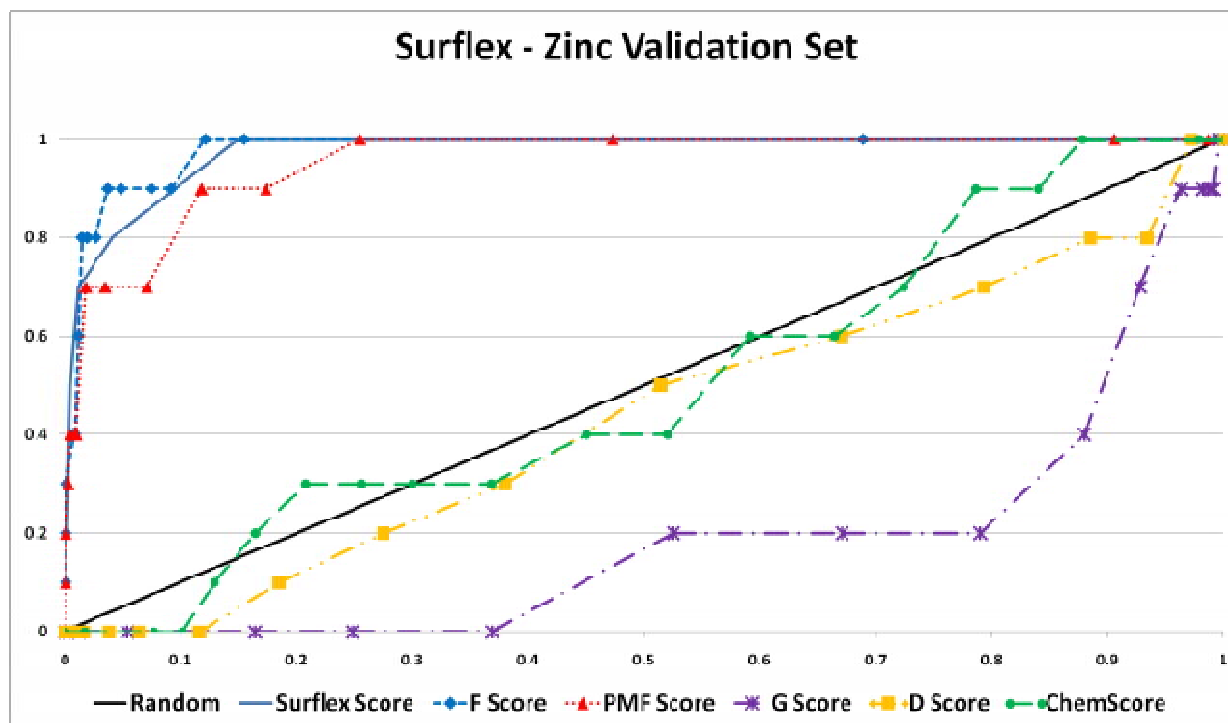
Figure 12S. ZINC Decoy Set, Enrichment at 2%
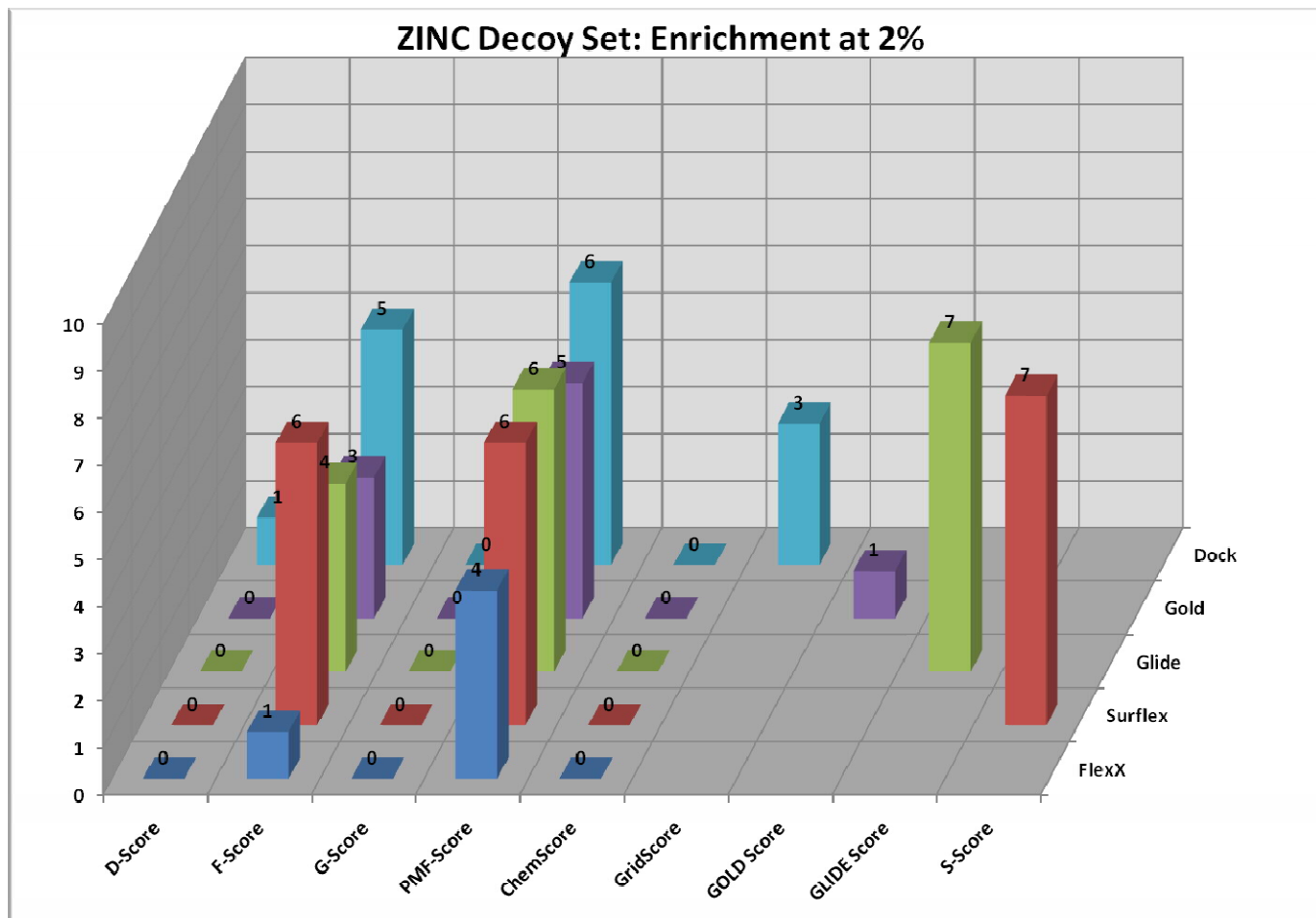

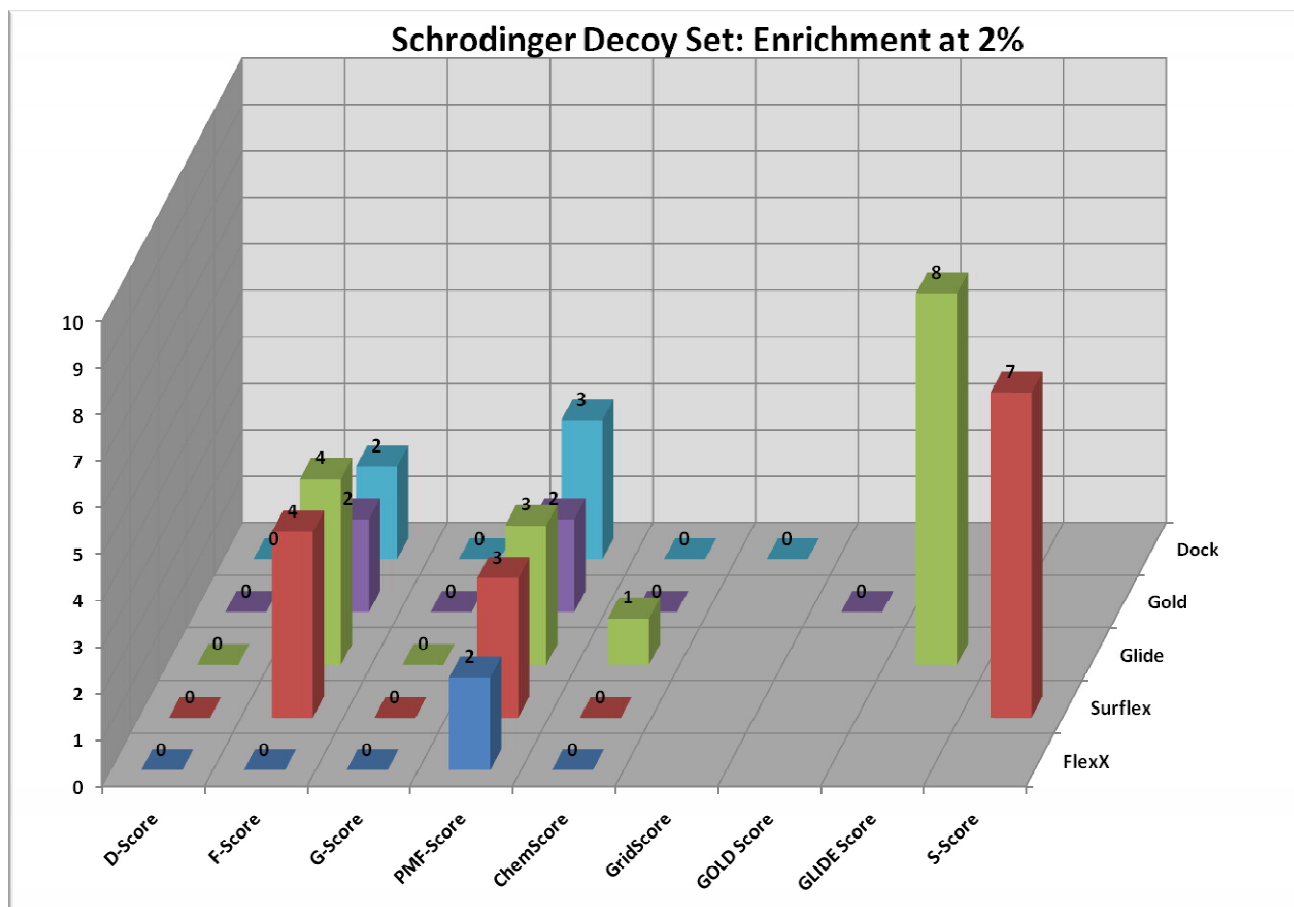
ZINC Decoy Set: Enrichment at 2%

Figure 13S. Schrodinger Decoy Set, Enrichment at 2%

Figure 14S. ACD Decoy Set, Enrichment at 2%

ACD Decoy Set: Enrichment at 2%