Electronic Supplementary Information
Computational biochemistry investigation to describe the binding energy interaction between an estrogen receptor and its agonists

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TABLE S1. Individual region binding energies of 17β-estradiol and diethylstilbestrol. Table is organized from the strongest interaction ($>$ 10 kcal mol^{-1}) to the weakest one ($<$ 5 kcal mol^{-1}).

Interaction strength (kcal mol^{-1})	Protein region and total energy (kcal mol^{-1})	
	17β-estradiol	Diethylstilbestrol
$>$ 10	H3 (-28.61)	H3 (-24.98)
	H11 (-10.74)	H11 (-13.91)
5 – 10	S1 (-6.31)	H6 (-7.66)
	H5 (-5.80)	H8 (-5.94)
	H8 (-5.48)	–
	–	–
$<$ 5	H6 (-4.48)	S1 (-4.81)
	H7 (-1.23)	H7 (-3.20)
	L7 (-0.84)	H5 (-1.86)
	H9 (-0.35)	L2 (-0.79)
	S2 (-0.10)	L7 (-0.19)
	H12 (0.03)	H9 (-0.14)
	L11 (0.04)	H2 (0.00)
	L2 (0.52)	S2 (0.08)
	H2 (0.68)	L11 (0.08)
	L6 (6.07)	L6 (0.33)
	–	H12 (2.87)

TABLE S2. Description of the 120 ERα residues interacting with E2. We also shown the functional groups and distances of the ligand to each amino-acid in the binding pocket radius ranging from 2.0 to 12.5 Å.

Residue	Atomic Group	Distance (Å)	Radius (Å)	Energy (kcal mol^{-1})	Residue	Atomic Group	Distance (Å)	Radius (Å)	Energy (kcal mol^{-1})
GLU353	i(C3)OH	1.96	2.0	-14.65	THR431	ii(C6)H	8.81	9.0	-0.06
PHE404	i(C2)H; i(ring); ii(C9)H	2.76; 4.91; 2.28	2.5	-6.24	VAL534	ii(C12)H; iii(C17)OH	6.46; 6.85	6.5	-0.05
LEU346	i(C1)H; ii(C11)H	2.84; 2.13	2.5	-6.13	ASN519	iii(C16)H	7.36	7.5	-0.05
HIS524	iii(C17)OH	2.07	2.5	-4.57	LEU544	iii(C18)H	6.35	6.5	-0.04
LEU391	i(C4)H; i(ring); ii(C6)H	1.94; 4.81; 2.45	2.0	-4.43	HIS513	ii(C7)H	9.93	10.0	-0.04
MET388	ii(C6)H; iii(C7)H	2.26; 2.21	2.5	-3.94	LEU536	iii(C18)H	6.53	7.0	-0.03
MET343	ii(C12)H; iii(C17)OH	2.31; 2.59	2.5	-3.90	SER341	ii(C12)H	9.46	9.5	-0.03
LEU525	iii(C18)H	2.54	3.0	-3.43	ILE452	ii(C6)H	9.96	10.0	-0.03
LEU384	ii(C8)H; iii(C15)H	2.24; 2.71	2.5	-3.35	ALA340	iii(C17)OH	9.57	10.0	-0.02
MET421	iii(C17)H	2.05	2.5	-1.98	TYR526	iii(C17)OH	6.47	6.5	-0.01
LEU387	i(C4)H; i(ring)	2.46; 3.29	2.5	-1.75	ILE514	ii(C6)H	7.46	7.5	-0.01
THR347	ii(C12)H	3.19	3.5	-1.70	VAL533	iii(C17)OH	7.63	8.0	-0.01
ALA350	i(C1)H; i(ring)	2.88; 5.15	3.0	-1.67	ASN407	i(C3)OH	10.07	10.5	-0.01
ILE424	iii(C15)H	2.38	2.5	-1.63	ASN532	iii(C17)OH	11.61	12.0	-0.01
LEU428	ii(C7)H	2.58	3.0	-1.63	GLY420	iii(C16)H	5.97	6.0	-0.0002
GLY521	iii(C16)H	2.35	2.5	-1.39	LEU429	iii(C15)H	8.29	9.0	0.00
ASP351	i(C2)H; ii(C11)H	6.15; 6.59	6.5	-1.35	SER338	ii(C12)H	11.07	11.5	0.01
GLU330	i(C2)H	9.23	9.5	-0.82	TRP360	i(C3)OH	11.95	12.0	0.01
GLY390	i(C4)H	4.98	5.0	-0.81	CYS381	ii(C6)H	11.54	12.0	0.01
GLU339	iii(C17)OH	8.10	8.5	-0.73	LEU379	iii(C18)H	12.01	12.5	0.01
LEU349	i(C2)H	2.53	3.0	-0.68	SER329	i(C2)H	6.57	7.0	0.02
GLU419	iii(C17)OH	6.92	7.0	-0.65	HIS398	i(C3)OH	12.08	12.5	0.02
LYS401	ii(C7)H	10.41	10.5	-0.62	ILE510	i(C2)H	12.25	12.5	0.02
LEU402	ii(C7)H	4.78	5.0	-0.50	SER527	iii(C17)OH	6.73	7.0	0.03
MET528	iii(C17)OH	3.39	3.5	-0.50	CYS530	iii(C17)OH	9.60	10.0	0.03
TRP383	iii(C18)H	4.18	4.5	-0.44	TYR331	i(C2)H	10.64	11.0	0.03
PHE435	i(C4)H	10.08	10.5	-0.42	VAL422	iii(C16)H	7.39	7.5	0.04
GLU523	iii(C16)H	6.17	6.5	-0.39	PHE445	i(C4)H	8.62	9.0	0.04
LEU345	i(C1)H; ii(C11)H	5.69; 6.00	6.0	-0.37	LEU541	iii(C18)H	9.96	10.0	0.04
LYS449	i(C4)H	8.77	9.0	-0.36	ILE386	i(C4)H; ii(C6)H	5.74; 6.22	6.0	0.05
ASN348	i(C2)H; ii(C11)H	6.68; 6.30	6.5	-0.33	LYS529	iii(C18)H	7.38	7.5	0.05
MET522	iii(C16)H	4.56	5.0	-0.33	ALA382	ii(C6)H	8.70	9.0	0.05
ARG515	iii(C15)H	9.37	9.5	-0.25	GLU380	iii(C18)H	11.34	11.5	0.05
MET517	ii(C7)H; iii(C15)H	5.64; 5.03	5.5	-0.23	ILE358	i(C3)OH	12.01	12.5	0.05
LYS520	iii(C16)H	4.80	5.0	-0.22	MET357	ii(C6)H	7.51	8.0	0.07
MET342	ii(C12)H	5.99	6.0	-0.22	PRO324	i(C3)OH	8.32	8.5	0.07
GLY415	iii(C17)H	7.72	8.0	-0.21	SER432	ii(C6)H	9.26	9.5	0.08
TRP393	i(C4)H	7.31	7.5	-0.20	PRO406	i(C3)OH	7.83	8.0	0.09
SER395	i(C4)H	6.89	7.0	-0.19	VAL355	i(C2)H	9.88	10.0	0.11
SER518	ii(C7)H; iii(C15)H	5.92; 5.07	5.5	-0.18	CYS417	iii(C17)OH	9.83	10.0	0.11
VAL418	iii(C17)OH	4.53	5.0	-0.18	LYS416	iii(C17)H	10.25	10.5	0.11
LEU539	ii(C11)H	11.27	11.5	-0.17	ASP545	iii(C18)H	11.48	11.5	0.11
ARG412	ii(C7)H	10.60	11.0	-0.16	LEU408	i(C2)H	5.80	6.0	0.12
LEU540	iii(C18)H	4.94	5.0	-0.15	ILE326	i(C3)OH	6.61	7.0	0.14
PHE425	iii(C14)H	4.45	4.5	-0.14	GLU423	iii(C16)H	7.65	8.0	0.14
PRO325	i(C3)OH	7.86	8.0	-0.14	HIS356	i(C3)OH	8.89	9.0	0.14
LEU410	ii(C9)H	6.46	6.5	-0.13	SER537	ii(C12)H	10.17	10.5	0.15
LEU354	ii(C11)H	6.37	6.5	-0.13	MET543	iii(C18)H	9.19	9.5	0.18
PHE337	ii(C12)H	9.41	9.5	-0.13	HIS547	iii(C18)H	10.09	10.5	0.19
MET427	iii(C15)H	6.82	7.0	-0.12	ALA405	i(C3)OH	6.03	6.5	0.20
GLY344	ii(C12)H	7.40	7.5	-0.12	LEU403	i(C3)OH	5.56	6.0	0.21
HIS516	iii(C15)H	8.41	8.5	-0.10	LEU327	i(C3)OH	6.09	6.5	0.25
LEU409	i(C3)OH	9.72	10.0	-0.10	GLU323	i(C3)OH	11.03	11.5	0.31
GLN414	iii(C17)OH	9.87	10.0	-0.10	ASP426	iii(C15)H	8.29	8.5	0.32
ILE389	i(C4)H; ii(C6)H	5.45; 5.54	5.5	-0.08	GLU385	i(C4)H; ii(C6)H	6.83; 6.21	6.5	0.43
MET396	i(C4)H	10.58	11.0	-0.08	LYS531	iii(C17)OH	8.73	9.0	0.80
ALA430	ii(C7)H	11.06	11.5	-0.08	TYR328	i(C2)H	8.05	8.5	0.68
GLU542	iii(C18)H	12.22	12.5	-0.08	ARG352	i(C2)H	6.99	7.0	3.22
PRO535	ii(C12)H	9.88	10.0	-0.07	ARG394	i(C3)OH	2.03	2.5	5.31
VAL392	i(C4)H	4.90	5.0	-0.06	ASP411	ii(C7)H	10.98	11.0	6.60

TABLE S3. Description of the 128 ERα residues interacting with DES. We also shown the functional groups and distances of the ligand to each amino-acid in the binding pocket radius ranging from 2.0 to 12.5 Å.

Residue	Atomic Group	Distance (Å)	Radius (Å)	Energy (kcal mol^{-1})	Residue	Atomic Group	Distance (Å)	Radius (Å)	Energy (kcal mol^{-1})
GLU353	i(C3)OH	1.73	2.0	-15.04	SER329	i(C4)H	8.95	9.0	-0.05
LEU346	ii(C8)H; iii(CP5)H	2.24; 2.71	3.0	-5.12	HIS513	ii(C9)H	10.12	10.5	-0.05
PHE404	i(C6)H; i(ring); ii(C8)H	2.88; 5.39; 2.31	2.5	-4.54	GLU380	ii(CP8)H	10.53	11.0	-0.05
LEU525	ii(CP9)H; iii(ring); iii(CP3)OH	2.93; 4.35; 2.27	2.5	-4.56	ALA430	ii(C9)H	10.16	11.5	-0.05
MET388	i(C2)H; i(ring); ii(C9)H	2.67; 5.95; 2.31	2.5	-3.65	LEU429	ii(C9)H	7.70	8.0	-0.04
LEU391	i(C2)H; i(ring); ii(C9)H	2.60; 4.99; 2.85	3.0	-3.59	LEU403	i(C3)OH	8.03	8.5	-0.04
HIS524	iii(CP2)H	2.39	2.5	-3.27	ILE452	i(C2)H	9.69	10.0	-0.04
ASP351	ii(CP9)H	5.23	5.5	-2.92	CYS530	iii(CP3)OH	8.45	8.5	-0.03
MET421	iii(CP4)H; iii(ring)	2.88; 3.03	3.0	-2.74	ASN413	ii(C9)H	12.10	12.5	-0.03
THR347	ii(CP8)H	2.87	3.0	-2.73	LYS529	iii(CP3)OH	5.98	6.0	-0.02
LEU384	i(C1)H; i(ring); ii(CP8)H	2.76; 5.72; 2.16	2.5	-2.62	ALA340	iii(CP4)H	8.80	9.0	-0.02
MET343	iii(CP4)H; iii(ring)	2.29; 5.99	2.5	-2.60	GLN414	ii(C8)H	10.17	10.5	-0.02
LYS416	ii(C9)H	10.58	11.0	-2.56	LEU690	ii(CP9)H	11.31	11.5	-0.02
GLY521	iii(CP2)H	2.37	2.5	-2.28	LEU453	i(C3)OH	12.07	12.5	-0.02
MET528	iii(CP3)OH	2.65	3.0	-1.70	SER338	iii(CP4)H	10.60	11.0	-0.01
ILE424	ii(C9)H	2.56	3.0	-1.53	GLY400	ii(C9)H	12.94	12.5	-0.01
ALA350	i(C5)H; i(ring); ii(CP9)H	2.49; 4.82; 2.27	2.5	-1.43	LYS520	iii(CP2)H	4.87	5.0	-0.004
TRP383	ii(CP9)H	2.70	3.0	-1.14	MET543	ii(CP9)H	6.87	7.0	0.00
LEU540	ii(CP9)H	2.33	2.5	-1.04	PHE337	ii(C8)H	11.34	11.5	0.00
LEU428	ii(C9)H	2.14	2.5	-0.88	ALA546	ii(CP9)H	11.37	11.5	0.00
PHE425	ii(C9)H	3.30	3.5	-0.85	TYR331	i(C5)H	11.67	12.0	0.00
MET522	iii(CP2)H	4.41	4.5	-0.84	VAL534	iii(CP4)H	6.20	6.5	0.01
GLU330	i(C4)H	10.42	10.5	-0.73	MET396	i(C2)H	11.36	11.5	0.01
SER432	ii(C9)H	9.91	10.0	-0.70	ASN407	i(C4)H	11.92	12.0	0.02
GLY390	i(C2)H	4.99	5.0	-0.68	LEU408	ii(C8)H	7.07	7.5	0.03
LEU345	i(C5)H	6.30	6.5	-0.51	ILE514	ii(C9)H	7.83	8.0	0.03
LYS401	ii(C9)H	10.47	10.5	-0.42	ILE510	i(C2)H	12.46	12.5	0.03
ARG412	ii(C9)H	9.16	9.5	-0.39	MET357	i(C3)OH	6.12	6.5	0.04
MET342	iii(CP5)H	6.30	6.5	-0.36	LEU541	ii(CP9)H	8.28	8.5	0.04
ASP538	ii(CP9)H	10.87	11.0	-0.34	TRP360	i(C3)OH	10.31	10.5	0.04
MET517	ii(C9)H	5.54	6.0	-0.32	LEU379	ii(CP9)H	10.96	11.0	0.04
LEU402	ii(C9)H	4.45	4.5	-0.30	LEU511	i(C2)H	11.98	12.0	0.04
ARG515	iii(CP1)H	10.19	10.5	-0.30	PRO324	i(C3)OH	8.57	9.0	0.06
LEU354	ii(CP9)H	4.29	4.5	-0.29	ILE326	i(C3)OH	8.36	8.5	0.07
VAL418	iii(CP3)OH	4.93	5.0	-0.28	ALA405	i(C3)OH	8.01	8.5	0.07
ILE386	i(C2)H	5.35	5.5	-0.28	PHE445	i(C3)OH	9.00	9.5	0.07
SER518	iii(CP1)H	5.60	6.0	-0.27	PRO406	i(C3)OH	9.88	10.0	0.09
GLY344	iii(CP4)H	6.81	7.0	-0.26	ILE358	i(C3)OH	10.21	10.5	0.09
MET427	ii(C9)H	7.11	7.5	-0.23	CYS381	ii(CP8)H	10.60	11.0	0.09
TYR328	i(C4)H	9.58	10.0	-0.23	VAL422	ii(C9)H	7.69	8.0	0.10
LEU536	iii(CP4)H	4.87	5.0	-0.20	GLU323	i(C3)OH	11.67	12.0	0.10
HIS516	iii(CP1)H	9.23	9.5	-0.18	TYR526	iii(CP3)OH	5.17	5.5	0.11
GLU542	ii(CP9)H	10.24	10.5	-0.18	ASP545	ii(CP9)H	10.54	11.0	0.11
GLY420	iii(CP3)OH	7.06	7.5	-0.17	ASN359	i(C3)OH	12.69	12.5	0.11
ILE389	i(C2)H	5.09	5.5	-0.15	ALA382	i(C2)H	8.79	9.0	0.14
VAL392	i(C2)H	5.32	5.5	-0.15	VAL355	i(C3)OH	8.89	9.0	0.14
GLY415	ii(C9)H	7.88	8.0	-0.15	LEU327	i(C3)OH	6.26	6.5	0.19
LYS449	i(C3)OH	8.62	9.0	-0.15	HIS356	i(C3)OH	8.20	8.5	0.19
LYS531	iii(CP3)OH	8.22	8.5	-0.14	SER527	iii(CP3)OH	4.72	5.0	0.20
PRO325	i(C3)OH	8.76	9.0	-0.14	GLU419	iii(CP3)OH	6.20	6.5	0.27
LEU544	ii(CP8)H	6.66	7.0	-0.13	ASN348	ii(CP9)H	6.01	6.5	0.31
SER341	iii(CP5)H	9.81	9.5	-0.13	SER537	ii(CP9)H	6.79	7.0	0.31
THR431	ii(C9)H	9.15	9.5	-0.12	LEU539	ii(CP9)H	8.63	9.0	0.37
ASN519	iii(CP2)H	7.40	7.5	-0.11	HIS547	ii(CP8)H	8.49	8.5	0.39
CYS417	iii(CP4)H	10.25	10.5	-0.11	GLU423	ii(C9)H	7.64	8.0	0.57
SER395	i(C2)H	7.87	8.0	-0.10	ASP411	ii(C9)H	9.76	10.0	0.64
VAL533	iii(CP4)H	7.73	8.0	-0.10	ASP426	ii(C9)H	7.49	7.5	0.68
ASN532	iii(CP3)OH	9.44	9.5	-0.06	ARG394	i(C3)OH	3.48	3.5	0.70
PRO535	iii(CP4)H	9.58	10.0	-0.06	GLU339	iii(CP4)H	7.84	8.0	0.71
PHE435	i(C2)H	10.25	10.5	-0.06	LEU349	i(C4)H	3.84	4.0	0.73
LEU409	ii(C8)H	10.78	11.0	-0.06	GLU385	i(C2)H	6.10	6.5	0.87
GLU523	iii(CP3)OH	5.44	5.5	-0.05	LEU387	i(C3)OH; i(ring)	2.29; 4.67	2.5	1.09
LEU410	ii(C8)H	6.18	6.5	-0.05	ARG548	iii(CP2)H	8.47	8.5	3.64
TRP393	i(C2)H	7.68	8.0	-0.05	ARG352	i(C4)H	6.82	7.0	4.07