Electronic Supplementary Material (ESI) for Molecular BioSystems.

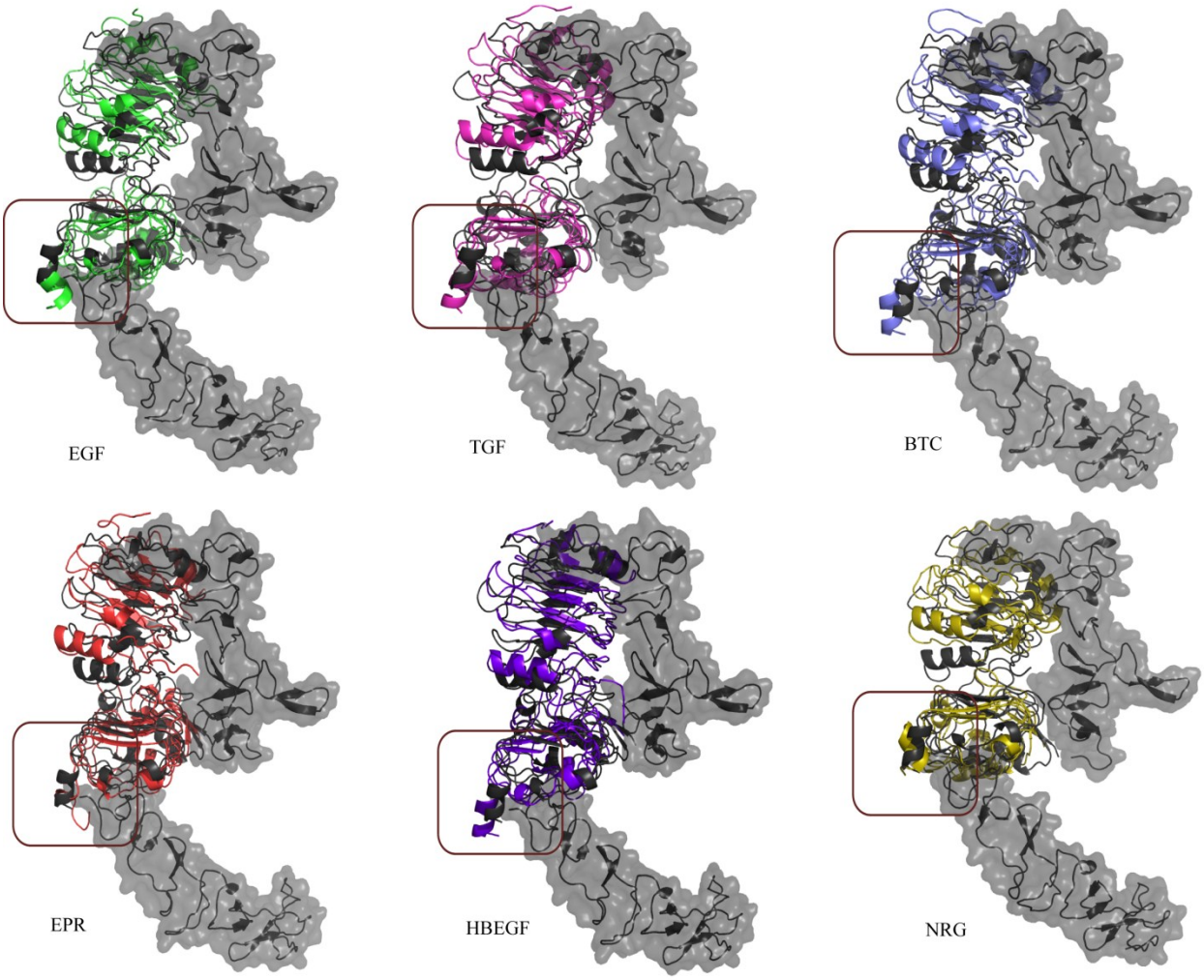

Figure S1. Fluctuation at domain III. After simulation, conformational changes in the domain III were shown. Especially in the squared part, there are some significant changes in the EGF, TGF, HBEGF and BTC complexes. But in EPR and NRG complexes, there are no much changes in domain III. (To view the superposition of domain I & III clearly, domain II & IV were viewed in surface with 50% transparent. After simulation, proteins are colored as follows: EGF - green, TGF - magenta, BTC - blue, EPR - orange, HBEGF - violet and NRG - yellow. Before simulation and domain II & IV of after simulation colored in black)

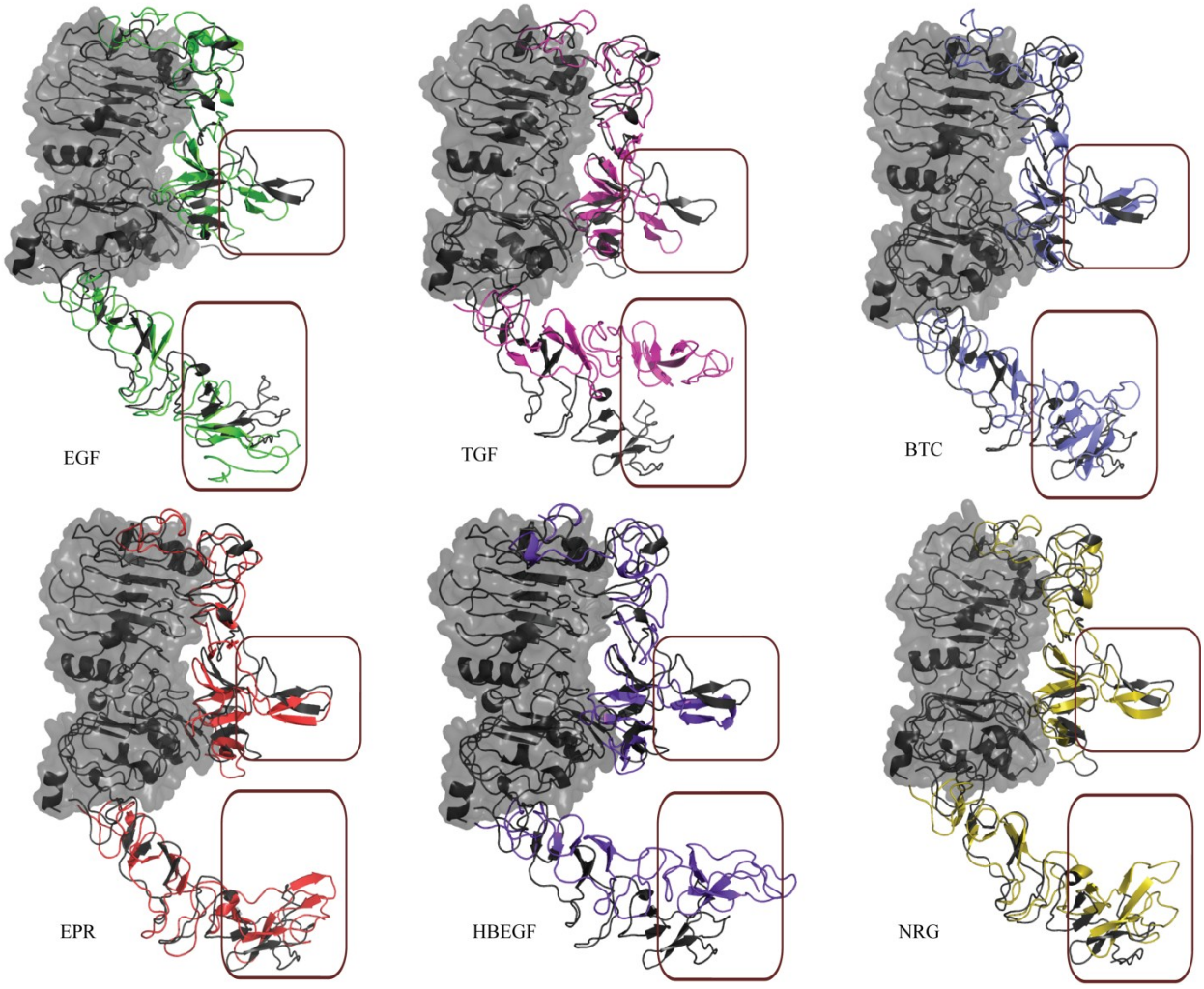

Figure S2. Fluctuation at domain II & IV. After simulation, conformational changes in the domain II & IV, which are involved in dimerization, were shown. As similar to Figure-7, especially in the squared part, there are some significant changes in the EGF, TGF, HBEGF and BTC complexes. But in EPR and NRG complexes, there are no much changes in domain II and IV as compared other complexes. (To view the superposition of domain II & IV clearly, domain I & III were viewed in surface with 50% transparent. After simulation, proteins are colored as follows: EGF - green, TGF - magenta, BTC - blue, EPR - orange, HBEGF - violet and NRG - yellow. Before simulation and domain I & III of after simulation colored in black)

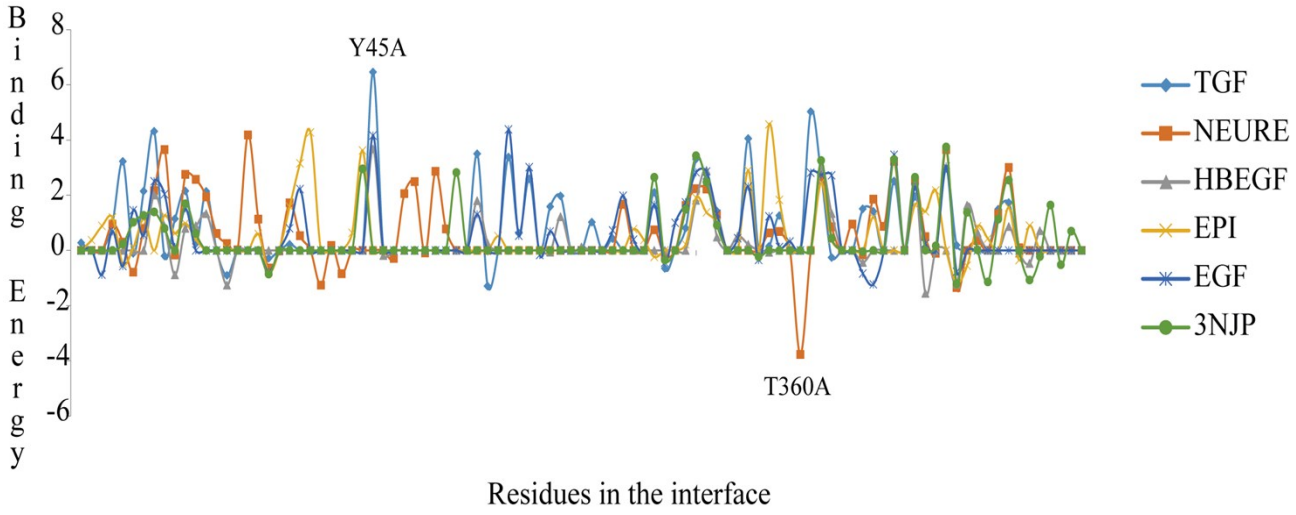

Figure S3. Alanine Scanning of wild EGFR with different type of peptides

Table S1. PatchDock docking results of EGFR1 complex.

	S.No	PatchDock Score	Area	glob	ACE	HB	No of Hydrogen Bonds	Lipophilic Interactions	Non-Bonded contacts	DCOMPLEX Kcal/mol
BTC	4	12660	1668.40	-59.07	-13.13	-3.94	8	29	111	-3.382604
	5	12630	1751.30	-26.74	7.76	-1.81	7	28	97	0.682373
	2	13548	1956.50	2.85	19.08	-5.95	3	37	142	0.182049
	3	12838	2029.80	61.38	7.01	-0.77	5	35	163	2.738081
	1	15072	2684.40	98.50	16.61	-3.69	11	44	242	10.006292
EGF	1	13592	1608.10	-121.44	-15.59	-5.55	3	35	77	-20.161909
	2	12380	1546.00	-22.51	1.85	-3.72	0	38	89	-10.966651
	5	11842	1441.60	-21.36	6.93	-3.23	4	24	78	-5.067156
	3	12280	1677.80	-18.10	-1.95	-6.57	6	34	106	-4.924673
	4	11870	1592.20	-17.72	1.89	-2.44	8	27	120	-3.884925
EPR	2	12960	1888.40	-59.57	-3.81	-7.38	8	33	109	-7.110625
	5	12628	1637.00	-47.28	5.94	-5.62	5	29	92	-8.157537
	3	12866	1654.10	-21.36	8.47	-6.75	5	31	114	-2.856983
	4	12864	1748.00	0.00	0.00	0.00	3	29	88	-4.700000
	1	13770	2012.70	257.47	-0.67	-8.84	7	36	182	2.119917
HBEGF	2	13068	1745.20	-56.56	6.06	-3.91	8	28	85	-5.736811
	3	12902	1803.40	-44.94	11.93	-4.96	4	34	111	-6.858859
	5	11874	1421.60	-11.30	5.77	-0.21	6	24	83	-6.988719
	1	13312	1760.90	1.71	7.49	-3.31	5	27	110	-2.546096
	4	12014	1641.10	5.04	8.16	-0.29	4	32	112	-2.228234
TGF	5	12040	1978.70	-68.76	4.75	-6.17	6	38	134	-2.940858
	2	12818	1867.10	-31.36	0.05	-1.10	4	36	139	-4.430787
	3	12458	1657.50	-29.94	9.50	-7.75	2	35	109	-0.618221
	4	12396	1612.70	-21.77	4.18	-7.26	4	33	95	-7.607943
	1	12830	1738.70	12.02	22.80	-8.73	1	37	99	2.444559
NRG	5	13894	2088.70	-13.49	13.55	-2.26	9	41	129	0.109678
	4	14276	1663.70	-8.19	12.55	-4.33	7	28	80	-4.849901
	3	14518	2459.70	25.97	11.91	-3.87	11	46	202	5.093046
	1	16304	2646.50	104.09	5.15	-9.25	13	36	210	9.391607
	2	15454	2667.80	111.41	16.21	-6.23	8	51	233	2.282157

Top 5 interactions of each PatchDock output were tabulated with their bonded and non-bonded contacts and binding affinities by using LIGPLOT v4.1 and DCOMPLEX.

Table S2. HADDOCK docking results of EGFR1 complex.

	Cluster No	HADDOCK Score	No.of Hydro Bond	No of Lipophilic Interactions	No of Non-bonded contacts	Vander Waals	Electrostatic	DCOMPLEX (kcal/mol)
BTC	1	-77.2 +/- 7.3	20	17	179	-62.1 +/- 8.3	-454.2 +/- 17.6	-21.004153
	7	-46.0 +/- 7.1	19	13	181	-80.1 +/- 3.6	-253.9 +/- 13.5	-18.485577
	2	-36.5 +/- 5.1	14	14	137	-68.8 +/- 5.4	-285.2 +/- 22.8	-16.497108
	4	-30.5 +/- 12.0	17	12	118	-56.1 +/- 7.0	-305.6 +/- 53.1	-14.015376
	3	-27.4 +/- 7.9	10	16	116	-59.7 +/- 4.3	-235.7 +/- 66.8	-15.179866
	5	-22.3 +/- 23.4	17	11	176	-63.9 +/- 13.6	-250.9 +/- 85.5	-16.832565
	6	-2.9 +/- 3.6	09	11	122	-61.7 +/- 7.3	-244.8 +/- 74.1	-11.727487
	8	11.8 +/- 4.8	09	12	107	-50.4 +/- 8.4	-102.3 +/- 39.0	-12.888943
EGF	1	-153.8 +/- 6.4	18	26	212	-90.4 +/- 4.2	-489.4 +/- 20.4	-27.680838
EPR	1	-109.9 +/- 9.1	20	15	192	-95.2 +/- 6.9	-396.2 +/- 36.8	-22.382473
	5	-61.4 +/- 14.1	17	22	190	-71.9 +/- 5.9	-282.9 +/- 21.9	-17.581910
	4	-59.3 +/- 7.5	11	15	129	-76.3 +/- 7.7	-264.4 +/- 37.7	-18.558986
	3	-57.3 +/- 6.5	12	25	169	-68.6 +/- 3.2	-250.4 +/- 9.3	-17.372820
	2	-44.8 +/- 3.0	15	16	148	-65.4 +/- 0.7	-201.0 +/- 27.3	-17.200911
	6	-39.7 +/- 4.3	16	12	137	-70.3 +/- 5.0	-335.4 +/- 37.4	-16.479005
	7	13.9 +/- 14.9	07	16	127	-51.8 +/- 3.4	-98.3 +/- 51.4	-12.317446
HBEGF	1	-95.0 +/- 16.9	17	21	172	-76.9 +/- 2.5	-337.7 +/- 66.5	-21.388598
	2	-45.2 +/- 5.7	17	18	143	-61.5 +/- 3.9	-390.8 +/- 29.2	-15.311818
	3	-19.5 +/- 5.3	15	14	177	-56.7 +/- 7.1	-264.5 +/- 39.8	-13.130677
	4	-16.7 +/- 12.3	13	15	179	-48.5 +/- 8.4	-327.9 +/- 48.7	-15.874752
TGF	1	-106.5 +/- 3.4	14	15	144	-81.4 +/- 4.8	-288.3 +/- 34.4	-21.107138
NRG	2	-26.4 +/- 20.2	17	16	33	-64.8 +/- 13.6	-343.5 +/- 17.3	-18.559786
	5	-20.6 +/- 12.5	23	06	20	-71.7 +/- 3.4	-408.5 +/- 65.3	-16.358490
	1	-18.5 +/- 4.5	12	19	43	-69.7 +/- 13.4	-205.0 +/- 60.5	-13.451252
	3	-16.4 +/- 1.7	16	09	21	-57.8 +/- 12.8	-342.1 +/- 82.7	-13.130585
	4	16.5 +/- 9.7	07	12	24	-52.5 +/- 6.6	-136.5 +/- 31.7	-8.822161
	7	17.5 +/- 6.6	11	19	37	-46.2 +/- 4.5	-286.7 +/- 95.8	-10.422640
	6	26.0 +/- 11.5	14	14	35	-53.8 +/- 4.4	-240.0 +/- 60.5	-11.338876

Collective list of HADDOCK output for each complex with their bonded and non-bonded contacts and binding affinities by using LIGPLOT v4.1 and DCOMPLEX.

Table S3. Residues involved in hydrogen bond interactions of each docked complexes.

S.No	EGFR1	EGF	TGF	BTC	HBEGF	EPR	NEURE
1	SER11						ASN30
2	ASN12		GLY40	ARG45		TYR36	ARG33, SER29
3	LYS13	GLU40				LEU46	
4	LEU14				LYS111		
5	THR15	CYS31, GLU40					SER29
6	GLN16	CYS31, ASN32, CYS33	ARG22, CYS32, CYS34		LEU127		SER3
7	GLY18	CYS33	CYS34	GLU44		CYS32	
8	GLU21			LYS10			LYS37
9	ASP22			LYS13		GLN18, LYS5	LYS37
10	SER26			GLU44			ARG33
11	ARG29				GLU141	ASN11, LEU15	CYS36
12	TYR45				LYS111		
13	TYR89	LYS28					
14	GLU90	LYS28					
15	TYR101		VAL1, GLU27				
16	HIS346	TYR44	HIS45			HIS43	
17	ARG353	CYS14	HIS18, GLU44	GLU36	ASP114	THR37	
18	ASP355	ARG41	ARG42		LYS113		
19	SER356				ARG110		
20	THR358				LYS113		
21	GLN384	HIS16, ARG45	ALA46	TYR38, GLY40	ASP114, ARG142	VAL39	
22	GLN408			ARG42, ILE39		GLU42	
23	HIS409				ARG142	GLU42, HIS16	
24	GLN411			ARG42		ASN11	
25	SER418			CYS32, CYS34		TYR13	GLU12
26	ASP436						ARG46
27	VAL437						ARG46
28	SER440	LEU47					THR14
29	LYS443				HIS118	GLN27	LYS11
30	LYS465	ASP46				MET10	PHE15, ARG46
31	SER468			PRO30, SER31	HIS139	ASN28	
32	SER474			GLU27			

Total number of residues involved in hydrogen bond interactions between EGFR1 and peptides before the simulation process.

Table S4. Residues involved in hydrogen bond interactions of each Simulated complexes.

S.No	EGFR1	EGF	TGF	BTC	HBEGF	EPR	NEURE
1	GLN8		ALA41			GLU42	
2	SER11		ALA41			GLU42, PHE44	
3	ASN12	GLY39, TYR37		ARG45			
4	LEU14			PHE49			
5	THR15	GLU40	ALA41	ARG45, PHE49, LEU48			
6	GLN16	CYS31, ASN32, CYS33	CYS 32, CYS34		TYR112, LEU127	VAL1	LEU179
7	GLY18	ASN32, CYS33	CYS34				
8	ASP22						LYS211
9	SER26			GLU44		GLY17	
10	ARG29						PHE216, GLY218
11	TYR45		CYS32				
12	SER99		GLU27				
13	TYR101		VAL1		ARG128		
14	ASP102		VAL1				
15	LEU325	GLN43					
16	HIS346	GLN43					
17	ALA351						SER206
18	ASP355		ARG42				
19	SER356	ASP11					ASP201
20	GLN384	ARG45	GLU44, ALA46	TYR38, GLY40			
21	GLN408			ALA41			
22	HIS409	TYR44					TYR208
23	SER418				HIS144	TYR13	GLU186
24	SER440				LEU146		PHE189
25	GLY441				TYR138		
26	ASN442			CYS32			
27	LYS443			ARG22, CYS32			
28	ASN469			SER31			
29	ASN473			GLU27			
30	SER474			GLU27			

Total number of residues involved in hydrogen bond interactions between EGFR1 and peptides after the simulation process

Table S5. Dynamic simulation analysis of EGFR with EGF-like peptides.

Str-Pro	Wild (nm)	BTC (nm)	EGF (nm)	EPR (nm)	HBEGF(nm)	NEURE (nm)	TGF (nm)
RMSD-Avg	0.626	0.639	0.530	0.568	0.748	0.500	0.831
RMSD-Small	0.001	0.000	0.001	0.001	0.000	0.000	0.000
RMSD-Large	0.832	0.940	0.745	1.042	1.040	0.787	1.186
Gyration-Avg	3.158	3.185	3.351	3.291	3.123	3.358	3.099
Gyration-Small	3.012	3.003	3.183	3.011	2.946	3.264	2.898
Gyration-Large	3.483	3.495	3.495	3.572	3.500	3.499	3.482
D1-D3-Avg	2.509	3.381	3.414	3.354	3.208	3.385	3.466
D1-D3-Small	2.227	3.184	3.272	3.219	3.050	3.224	3.241
D1-D3-Large	3.294	3.596	3.575	3.618	3.619	3.699	3.653
D2-D4-Avg	4.802	5.373	6.056	5.775	4.993	6.003	4.849
D2-D4-Small	4.065	4.631	5.374	4.376	4.154	5.435	4.001
D2-D4-Large	5.475	6.276	6.766	7.007	6.242	6.525	6.358
SASA-Avg	159.825	164.634	164.201	165.132	163.452	169.732	164.125
SASA-Small	149.597	157.112	154.816	155.048	153.259	160.694	155.473
SASA-Large	187.943	196.281	191.411	190.223	190.846	190.002	186.020
HBOND-Avg	NA	13.923	14.186	12.089	9.331	10.963	13.522
HBOND-Small	NA	4.000	4.000	4.000	2.000	1.000	5.000
HBOND-Large	NA	24.000	26.000	22.000	18.000	23.000	23.000
RMSF-Avg	0.253	0.308	0.251	0.385	0.301	0.295	0.336

Table S6. Dynamic domain analysis of bound and unbound EGFR1.

	EGFR1 vs EGFR1-EGF		EGFR1 vs EGFR1-TGF	EGFR1 vs EGFR1-HB-EGF	
Rotation Angle (deg)	20.4	60.5	77.9	30.1	59.4
Translation (Å)	-3.2	4.4	-1.5	-3.0	1.4
Closure (%)	99.9	99.5	83.4	85.0	51.7
Bending Residues	THR187-GLN194	ILE562-ASP563	VAL505-SER506	ASN274-VAL277	LYS516-LEU517, PRO522-GLU524, CYS534-GLU537

Conformational changes in bound EGFR1 are analysed with unbound EGFR1 through DynDom server