Supporting Information: Detailed methodology

A1 Ligand test-set construction

β-secretase: A structurally diverse set of known β-secretase (BACE) inhibitors was compiled using compounds extracted from the BindingDB [1], a publicly-available database of experimentally-measured protein-ligand binding affinities. As of September 2008, the BindingDB contained 174 ligands with well-defined BACE-1 IC_{50} data. Pipeline Pilot (see main text Ref. [51]) was used to filter out compounds with IC_{50} greater than 1 μM and/or molecular weight greater than 650 Da. From the remaining 67 active ligands, a diverse subset of 20 BACE inhibitor compounds (the "core" subset) was derived using the Diverse Molecules component of Pipeline Pilot. This implements a maximal dissimilarity procedure based on Tanimoto distance between ECFP6 (atom-type extended-connectivity) fingerprints.

On inspection, eight distinct chemotypes were present in this core subset. After discarding one chemotype which had no further representatives in the BindingDB, the structural diversity of the remaining chemotypes was quantified by taking the compound with lowest IC_{50} from each and then calculating Tanimoto similarity coefficients for the EPFP6 (atom-type path-based) fingerprints using Pipeline Pilot's Diversity FP Distances component. Amongst all possible pairs, the closest similiarity coefficient was 0.76 and the mean was 0.34. Representative molecules from each of the seven chemotypes are shown in Figure 1.

Eight or nine compounds from each of the seven chemotypes were then manually selected to create a reasonably-sized but diverse and chemotypically-balanced set of 59 BACE-active compounds [2, 3]. Since the IC_{50} values of these compounds were measured in different assays, it would be inappropriate to attach any significance to their IC_{50} rank ordering. However, for the current purposes of investigating enrichment what is important is that these compounds are *active* as opposed to *inactive*. The restrictive $IC_{50} < 1$ μM filter is designed to ensure this, regardless of which assay was used.

Structure-based virtual screening is operationally most valuable when it is able to distinguish active and inactive compounds that cannot be distinguished using simple "one-dimensional" descriptors alone. In an attempt to focus the evaluation in this direction, a key design principle was that the decoy set should possess similar molecular weight (MW) and logP distributions to the active set [4], as well as being structurally diverse. This ruled out the use of pre-compiled decks of "drug-like", i.e. Lipinski-compliant, decoys. Therefore, a bespoke property-matched decoy set was compiled using the publicly-accessible ZINC database of commerically-available compounds [5].

The first step in this process was the calculation of molecular weight and AlogP [6] histograms for the BACE active set. These formed "target" histograms for the decoy set, after being scaled by a constant factor such that the total area under the histograms was raised to 1500 compounds rather than the 59 compounds in the active set. The entire ZINC database [version 8] of more than 8 million

compounds was then pre-filtered to leave those with molecular weights likely to match those of the typically rather heavy BACE inhibitors. In particular, the ∼25000 compound Tanimoto T<0.6 selection of the ZINC "Everything" subset (#10) was enriched in heavier compounds by adding a subset derived from a 500<MW<1000 filter of the full Everything subset. This filtering was performed on the SMILES strings using Pipeline Pilot. Each compound was then considered in turn and accepted or rejected depending on whether it filled vacant positions in both the MW *and* logP histograms. The Diverse Molecules component was then used to derive a set of 500 structurally dissimilar property-matched decoy molecules.

Visual inspection of these compounds showed that 92 were either obvious multimers of smaller molecules, or were highly peptidic in character, or had long aliphatic side-chains, or had more than 4 fused rings. Removal of these compounds gave a cleaner set of 408 decoys with maximum Tanimoto coefficient between EPFP6 fingerprints of 0.72 and a mean of 0.27. Tanimoto coefficients of EPFP6 fingerprints were also used to quantify the structural similarity between actives and decoys. For each active the highest coefficient with any decoy was recorded, with the overall closest similarity being 0.67 and a mean closest similarity of 0.33.

cAbl: A diverse set of cAbl inhibitors was compiled using an approach almost identical to that adopted for BACE above. The main difference was that molecules active against cAbl were extracted from an in-house compound collection rather than from the BindingDB. The corporate collection contained about 3500 compounds which had both an IC_{50} of less than 1 μM in an enzymatic cAbl inhibition assay and a molecular weight between 200 Da and 600 Da. As above, the Diverse Molecules component of Pipeline Pilot was used to identify a "core" subset of 20 inhibitors. The closest EPFP6 Tanimoto similarity amongst all members of this core subset (see above) was 0.43 and the mean was 0.26. Since the structural diversity of this 20-member cAbl core subset was therefore greater than that of the 7-member BACE core subset, each of the twenty molecules in the cAbl subset was considered as a distinct chemotype.

The compounds which had not been selected for the core subset (but which passed the molecular weight and IC_{50} filters) were then automatically assigned to the chemotype with which they had highest scaffold EPFP6 Tanimoto similarity, as long as that similarity was above 0.6. Compounds with low similarity against all chemotypes were discarded. In total, 898 compounds were thus assigned to the twenty chemotypes. The six chemotypes which had acquired fewer than 10 representatives were rejected. For each of the remaining 14 chemotypes, the Diverse Molecules component was used to select 10 representatives, leaving a final set of 140 cAbl-active compounds.

The procedure described above for BACE was again used to derive a property-matched decoy set for the cAbl actives. In this case, however, the ∼25000 compound Tanimoto T<0.6 selection of the ZINC "everything" subset (#10) was sufficient and did not need to be enriched in heavier compounds (the cAbl actives have significantly lower molecular weight compared to those for BACE). The Diverse Molecules component was then used to derive a set of 400 structurally dissimilar property-matched decoy

molecules. After cleaning up (see above) this left 397 compounds with maximum Tanimoto coefficient between EPFP6 fingerprints of 0.62 and a mean of 0.25. Tanimoto coefficients of EPFP6 fingerprints were also used to quantify the structural similarity between actives and decoys. For each active the highest similarity coefficient with any decoy was recorded, with the overall closest similarity being 0.52 and a mean closest similarity of 0.34.

A2 Crystal-structure selection

β-secretase: In order to assemble a pool of crystallographically-derived protein conformations from which receptor ensembles could be constructed, BACE structures were downloaded from the RCSB Protein Data Bank [7]. To keep the docking calculations and subsequent analysis manageable, it was important that this pool was as small as possible whilst still covering the important conformational space of the BACE active site. An initial set of 10 downloaded crystal structures was therefore chosen to include the range of available resolutions (1.5 Å to 2.8 Å) and bound ligands of different chemotypes (peptidomimetic, nonpeptidomimetic, and apo). Principal Component Analysis (PCA) [8] was then used to map out the major structural differences in terms of a small number of collective coordinates, i.e. the high variance principal components. For this purpose an R-script was written to perform PCA on the cartesian coordinates of atoms in PDB files. In order to focus on structural variation in the BACE active site, the PCA was restricted to C_α atoms of following active site residues: Lys9 to Gln12 inclusive (10s) and Val69 to Gly74 inclusive (flap) – augmenting this subset with the additional active-site residues Ile29 to Gly34 inclusive, Lys107 and Phe108, and Ser225 to Thr231 inclusive produced negligible change in the PCA. Downloaded PDB files were first prepared in Maestro (see main text Rf. [44]) by deletion of any duplicate protein chains and alignment based on all residues using the Protein Structure Alignment tool. The modified PDB files were then submitted to the R-script.

This PCA of the initial set showed significant structural variation in only the flap (first principal component; residues 69 to 74) and, independently, the 10s loop (second principal component; residues 9 to 12) [9]. It was further revealed that, whilst variation in the 10s loop was well sampled by this initial set (4 structures were 10s "open" and 4 were 10s "closed"), there were only two flap-open structures (1SGZ and 1W50). The initial set was therefore augmented with four additional flap-open structures. A PCA was then performed on this final set of structures as described above, and a plot of the projections along the first two principal components is shown in Figure 3. Larger values of PC1 correspond to flap-open structures, and larger values of PC2 to 10s-open structures.

cAbl: As for BACE, crystal structures of the cAbl kinase domain were downloaded from the RCSB Protein Data Bank [7]. The approach described above was used to perform PCA on a subset of 13 of these crystal structures chosen to cover the range of available resolutions (1.7 Å to 2.7 Å) and to include kinase-active (6), inactive (5), and intermediate (2) conformations. A PCA restricted to the C_α atoms

of the following active-site residues was then performed: Lys247 to Tyr257 inclusive (glycine-rich loop), Ile314 to Gly321 (hinge), and Lys378 to Pro402 (DFG/activation loop). By construction this subset was composed of almost equal numbers of active and inactive conformations, and unsurprisingly the first principal component therefore corresponded to the switch in position of the activation loop. The only other significant structural variation was that of the conformation of the glycine rich loop. A second PCA was performed using only the C_α atoms of this region, and the resulting projections along the first two principal components are plotted in Figure 5. In broad terms, more negative values of the first principal component correspond to more extended ("tongue-like") conformations of the Glycine-rich loop. More positive values of the second principal component correspond to "W" rather than "U" conformations of the loop.

A3 Docking protocol

β-secretase: All test-set ligands were prepared for docking using the same preparation procedure. First, hydrogen atoms were removed and then added back in Maestro before being submitted to LigPrep (see main text Ref. [45]). Default LigPrep settings were used, except that specified chiralities were retained and a maximum of eight stereoisomers were generated for each compound by varying the configuration at unspecificed chiral centres. This resulted in 1847 stereoisomers/tautomers being generated from the original 467 compound test set.

Following this treatment, Maestro's Protein Preparation Wizard was used to prepare the chosen set of crystal structures for conversion to docking receptor grids. Default settings were used, except that disulphide bonds were detected and assigned. Following optimization of hydrogen bonding networks with the H-bond Assignment module, one of the catalytic aspartic acid residues (Asp32 [9]) was protonated before the structures were minimized with the Impref module (default settings). Glide receptor grids were then generated from the prepared protein structures, with the grids centred at the mean position of residues Asp32 (protonated), Thr72, and Asp228 [9]. In all other respects the default settings were used and no constraints were defined.

Docking of the test-set into each receptor grid was performed using Glide in SP mode (see main text Ref. [48]). Default Glide settings were used, except that nonplanar amide bonds were allowed since this had resulted in improved enrichment in preliminary tests. After docking, five poses for each of the 1847 test set stereoisomers/tautomers were selected for energy minimization using a dielectric constant of 2.0 and 100 iterations. At this point, only the top-scoring pose for each of the 467 test set compounds was retained. Sorting in order of increasing GlideScore (decreasingly favourable interactions) created the ranked list. Ensemble docking then simply corresponds to merging the ranked lists of the constituent receptors. Various rules can be used to perform this operation [10, 11]. In this work, of the multiple poses for each test-set compound (one in each constituents' ranked list), that with the most favourable docking

score is selected [12]. In the case of Glide, this is the pose assigned the most negative GlideScore. The result is a ranked list for the ensemble. The Maestro file containing the resulting poses was converted to SD format for further processing by Pipeline Pilot (see Section 2.4).

cAbl. The docking protocol used for cAbl was very similar to that described for BACE, and only the differences are noted here. Ligand preparation produced 912 ligand "states" from the original 537 compounds in the test set. Glide receptor grids were centred at the mean position of residues Gly251, Asp381, and Thr315 [13] and, in order to comfortably cover the entire cAbl active site, had sides of length 22 Å rather than the default of 20 Å which was used for BACE.

A4 Induced-Fit Docking protocol

We use the Induced-Fit Docking protocol provided by Schrödinger in Maestro (see main text Refs. [44] and [54]). Default settings were used. The Glide docking grids were centred as described above for the standard single-receptor dockings. In the initial docking step we did not remove any side-chains, therefore making it a simple soft-docking run in which the protein and ligand van der Waals potentials were scaled by a factor 0.5. In the side-chain optimization step, only residues with 5 Å of the ligand pose were modified.

A5 Enrichment metrics: Comparing an AUC to a mean AUC

In order to compare the AUC of an ensemble to the mean AUC of its constituent receptors (see Section 3.2 and Table 6) Eqs. 7 to 11 of Section 2.4 need to be modified. In particular, Eq. 7 becomes

$$\Delta\mathrm{AUC} = \mathrm{AUC_A} - \frac{1}{n}\sum_{i=1}^{n} \mathrm{AUC_{Bi}}, \tag{A1}$$

where, in the current context, $\mathrm{AUC_A}$ is the AUC of the ensemble and the $\{\mathrm{AUC_{Bi}}\}$ are the AUC values of the n constituents of the ensemble. From Eq. 2

$$\frac{1}{n}\sum_{i=1}^{n} \mathrm{AUC_{Bi}} = \frac{1}{n}\sum_{i=1}^{n} \langle \mathrm{TPR}\rangle_{\mathrm{decoys,Bi}} = \frac{1}{n}\sum_{i=1}^{n} \frac{1}{N_{\mathrm{decoys}}} \sum_{j=1}^{\mathrm{decoys}} \mathrm{TPR}_{j,\mathrm{Bi}}. \tag{A2}$$

Rearranging the order of summation gives

$$\begin{aligned} \frac{1}{n}\sum_{i=1}^{n} \mathrm{AUC_{Bi}} &= \frac{1}{N_{\mathrm{decoys}}} \sum_{j=1}^{\mathrm{decoys}} \frac{1}{n}\sum_{i=1}^{n} \mathrm{TPR}_{j,\mathrm{Bi}}, \\ &= \frac{1}{N_{\mathrm{decoys}}} \sum_{j=1}^{\mathrm{decoys}} \overline{\mathrm{TPR}}_{j,\mathrm{B}}, \end{aligned} \tag{A3}$$

where $\overline{\mathrm{TPR}}_{j,\mathrm{B}}$ is the mean TPR of the jth decoy at the n constituent receptors of the ensemble. Thus, using the notation of the main text,

$$\frac{1}{n}\sum_{i=1}^{n} \mathrm{AUC}_{\mathrm{Bi}} = \left\langle \overline{\mathrm{TPR}} \right\rangle_{\mathrm{decoys,B}} . \tag{A4}$$

So the modified Eq. 7 can be expressed as

$$\Delta\mathrm{AUC} = \left\langle \mathrm{TPR} \right\rangle_{\mathrm{decoys,A}} - \left\langle \overline{\mathrm{TPR}} \right\rangle_{\mathrm{decoys,B}} , \tag{A5}$$

and following the argument presented in the main text leads to the equivalent of Eq. 8

$$\Delta\mathrm{AUC} = \left\langle \mathrm{TPR}_{\mathrm{A}} - \overline{\mathrm{TPR}}_{\mathrm{B}} \right\rangle_{\mathrm{decoys}} . \tag{A6}$$

Alternatively, inserting Eq. 3 in Eq. A1 gives

$$\Delta\mathrm{AUC} = \left\langle \overline{\mathrm{FPR}}_{\mathrm{B}} - \mathrm{FPR}_{\mathrm{A}} \right\rangle_{\mathrm{actives}} . \tag{A7}$$

From this point on the analysis follows the same path as the main text, i.e. the variances associated with the means in Eqs. A6 and A7 are

$$\mathrm{Var}_{\Delta,\mathrm{d}} = \frac{1}{N_{\mathrm{decoys}}} \sum_{j}^{\mathrm{decoys}} \left(\left(\mathrm{TPR}_{\mathrm{j,A}} - \overline{\mathrm{TPR}}_{\mathrm{j,B}} \right) - \left\langle \mathrm{TPR}_{\mathrm{A}} - \overline{\mathrm{TPR}}_{\mathrm{B}} \right\rangle_{\mathrm{decoys}} \right)^2 , \tag{A8}$$

$$\mathrm{Var}_{\Delta,\mathrm{a}} = \frac{1}{N_{\mathrm{actives}}} \sum_{j}^{\mathrm{actives}} \left(\left(\overline{\mathrm{FPR}}_{\mathrm{j,B}} - \mathrm{FPR}_{\mathrm{j,A}} \right) - \left\langle \overline{\mathrm{FPR}}_{\mathrm{B}} - \mathrm{FPR}_{\mathrm{A}} \right\rangle_{\mathrm{actives}} \right)^2 . \tag{A9}$$

The standard error in Eq. 12 and the p-value in Eq. 13 then give the desired comparison of an AUC of an ensemble to the mean AUC of its constituent receptors. Note that the rearrangement of the summations in Eq. A3 can only be performed if exactly the same set of decoys (or actives for Eq. A7) are docked to *all* of the n receptors. This condition is not always met for the comparisons made in this work due a small number test-set compounds failing to dock to some of the receptors. In this case, the mean AUC of the ensemble's constituents is calculated using the subset of test-set compounds that successfully dock to all of the constituent receptors.

References

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Supporting Information: Detailed results

Contents:

Table S1: A version of Table 1 expanded to include an estimate of the AUC standard error (SE; calculated using Eq.(6)) and the Mean GlideScore (MGS). The latter metric is simply the mean docking score (GlideScore) of the top 1% of compounds in the ranked list [Rao *et al*, J. Comput.-Aided Mol. Des. (2008), **22**, 621-627].

PDB	AUC	SE	MGS
2Q11	0.778	0.034	-9.921
1XS7	0.751	0.041	-10.377
1SGZ	0.743	0.033	-9.160
1M4H	0.743	0.043	-11.947
2VA7	0.732	0.044	-8.392
2IQG	0.732	0.042	-11.318
2VJ7	0.728	0.041	-11.214
2QU2	0.726	0.034	-8.331
3E3W	0.719	0.044	-8.859
1YM4	0.718	0.046	-11.093
1FKN	0.714	0.044	-10.505
2QP8	0.701	0.044	-10.555
1W50	0.688	0.046	-7.512
1W51	0.679	0.050	-10.944

Table S2: A version of Table 3 expanded to include an estimate of the AUC standard error (SE; calculated using Eq.(6)) and the Mean GlideScore (MGS). The latter metric is simply the mean docking score (GlideScore) of the top 1% of compounds in the ranked list [Rao *et al*, J. Comput.-Aided Mol. Des. (2008), **22**, 621-627].

PDB	AUC	SE	MGS	Conformation
2QOH	0.910	0.014	-10.832	Active
3CS9	0.897	0.015	-11.658	Inactive
2HYY	0.888	0.016	-10.956	Inactive
2GQG	0.882	0.015	-9.979	Active
2HIW	0.869	0.017	-11.282	Inactive
1IEP	0.867	0.017	-11.116	Inactive
1FPU	0.866	0.017	-10.823	Inactive
1M52	0.858	0.018	-10.205	Active
2HZI	0.856	0.020	-11.668	Active
2HZ0	0.835	0.023	-11.751	Intermediate
2G2H	0.828	0.019	-9.466	Active
2G2F	0.822	0.020	-8.255	Active
2G1T	0.671	0.024	-7.954	Intermediate

Table S3: The AUC metric, AUC standard error estimate (SE; calculated using Eq.(6)), Mean GlideScore (MGS), and ensemble construction strategy (see Table 5) for the BACE ensembles. The MGS metric is simply the mean docking score (GlideScore) of the top 1% of compounds in the ranked list [Rao *et al*, J. Comput.-Aided Mol. Des. (2008), **22**, 621-627].

Ensemble	AUC	SE	MGS	Construction Strategy
2Q11+1SGZ	0.792	0.029	-9.921	A
2Q11+2VA7	0.784	0.032	-9.921	A
1SGZ+2VA7	0.777	0.033	-9.160	A
1XS7+1M4H	0.749	0.042	-11.947	A
1FKN+2QP8	0.707	0.045	-10.644	A
1XS7+1FKN	0.761	0.041	-10.669	A
1M4H+1FKN	0.742	0.043	-11.947	A
1M4H+2QP8	0.718	0.046	-11.947	A
2IQG+2VJ7	0.728	0.043	-11.532	A
2IQG+1YM4	0.725	0.044	-11.448	A
2QU2+3E3W	0.781	0.034	-8.991	A
2QU2+1W50	0.736	0.035	-8.331	A
3E3W+1W50	0.714	0.045	-8.859	A
2Q11+1XS7	0.791	0.033	-10.440	B
2Q11+2IQG	0.778	0.035	-11.318	B
2Q11+2QU2	0.788	0.031	-9.921	B
1XS7+2IQG	0.729	0.044	-11.357	B
1XS7+2QU2	0.800	0.035	-10.377	B
2IQG+2QU2	0.767	0.038	-11.318	B
2Q11+1W51	0.787	0.035	-10.944	C
1XS7+1W51	0.741	0.044	-11.008	C
1SGZ+1W51	0.784	0.035	-10.944	C
1M4H+1W51	0.709	0.048	-11.962	C
2VA7+1W51	0.702	0.049	-10.944	C
2IQG+1W51	0.716	0.046	-11.386	C
2VJ7+1W51	0.743	0.043	-11.367	C
2QU2+1W51	0.761	0.039	-10.944	C
3E3W+1W51	0.706	0.048	-10.944	C
1YM4+1W51	0.720	0.048	-11.226	C
1FKN+1W51	0.712	0.048	-10.944	C
2QP8+1W51	0.711	0.047	-10.967	C
1W50+1W51	0.674	0.051	-10.944	C
2Q11+1XS7	0.791	0.033	-10.440	D
2Q11+1SGZ	0.792	0.029	-9.921	D
2Q11+1M4H	0.802	0.034	-11.947	D
2Q11+2VA7	0.784	0.032	-9.921	D
2Q11+2IQG	0.778	0.035	-11.318	D
2Q11+2VJ7	0.754	0.036	-11.214	D
2Q11+2QU2	0.788	0.031	-9.921	D
2Q11+3E3W	0.803	0.029	-9.921	D
2Q11+1YM4	0.770	0.038	-11.093	D
2Q11+1FKN	0.781	0.035	-10.505	D
2Q11+2QP8	0.759	0.037	-10.555	D

2Q11+1W50	0.778	0.034	-9.921	D
2Q11+1W51	0.787	0.035	-10.944	D
2VA7+2QU2	0.787	0.035	-8.557	E
1YM4+2QU2	0.777	0.037	-11.093	E
2QU2+1SGZ	0.755	0.032	-9.219	E
1XS7+2QU2+1SGZ	0.820	0.030	-10.377	E
3E3W+2QU2+1SGZ	0.791	0.030	-9.301	E
1M4H+2QU2+1SGZ	0.824	0.032	-11.947	E
2Q11+2QU2+1SGZ	0.796	0.028	-9.921	E

Table S4: Comparing the virtual screening performance of the BACE ensembles to that of their individual constituent receptors: ΔAUC (Eq.9), the standard error estimate for ΔAUC (SEΔ; Eq.12), and the resulting *p*-value (Eq.13). "Mean" refers to the mean AUC of the ensemble's constituents – it is these comparisons that are used to judge whether ensembles are "better than average" (see Table 6). The *p*-values below 0.05 are marked with a star to emphasize significance at the 95% level.

Ensemble	Constituents	ΔAUC	SEΔ	p-value
2Q11+1SGZ	2Q11	0.015	0.013	0.265
	1SGZ	0.049	0.032	0.118
	Mean	0.032	0.014	0.026*
2Q11+2VA7	2Q11	0.006	0.010	0.539
	2VA7	0.052	0.035	0.145
	Mean	0.029	0.018	0.101
1SGZ+2VA7	1SGZ	0.034	0.012	0.003*
	2VA7	0.045	0.034	0.186
	Mean	0.040	0.016	0.012*
1XS7+1M4H	1XS7	-0.003	0.010	0.775
	1M4H	0.006	0.015	0.713
	Mean	0.001	0.007	0.845
1FKN+2QP8	1FKN	-0.006	0.015	0.679
	2QP8	0.006	0.013	0.633
	Mean	0.000	0.009	0.997
1XS7+1FKN	1XS7	0.010	0.014	0.479
	1FKN	0.047	0.020	0.016*
	Mean	0.028	0.010	0.005*
1M4H+1FKN	1M4H	-0.001	0.008	0.910
	1FKN	0.028	0.014	0.043*
	Mean	0.014	0.006	0.029*
1M4H+2QP8	1M4H	-0.025	0.014	0.072
	2QP8	0.017	0.014	0.221
	Mean	-0.004	0.009	0.644
2IQG+2VJ7	2IQG	-0.004	0.017	0.811
	2VJ7	0.000	0.012	0.983
	Mean	-0.002	0.010	0.844
2IQG+1YM4	2IQG	-0.007	0.017	0.690
	1YM4	0.008	0.009	0.418
	Mean	0.001	0.007	0.937
2QU2+3E3W	2QU2	0.055	0.025	0.025*
	3E3W	0.063	0.030	0.036*
	Mean	0.059	0.016	0.000*
2QU2+1W50	2QU2	0.010	0.009	0.249
	1W50	0.047	0.041	0.243
	Mean	0.029	0.020	0.149
3E3W+1W50	3E3W	-0.005	0.001	0.001*
	1W50	0.025	0.022	0.248
	Mean	0.010	0.011	0.349
2Q11+1XS7	2Q11	0.014	0.016	0.402
	1XS7	0.040	0.027	0.143

	Mean	0.027	0.013	0.041*
2Q11+2IQG	2Q11	0.001	0.011	0.964
	2IQG	0.046	0.026	0.078
	Mean	0.023	0.012	0.046*
2Q11+2QU2	2Q11	0.011	0.007	0.139
	2QU2	0.062	0.034	0.068
	Mean	0.036	0.016	0.023*
1XS7+2IQG	1XS7	-0.022	0.013	0.078
	2IQG	-0.003	0.011	0.815
	Mean	-0.012	0.007	0.097
1XS7+2QU2	1XS7	0.049	0.020	0.016*
	2QU2	0.074	0.032	0.019*
	Mean	0.061	0.015	0.000*
2IQG+2QU2	2IQG	0.035	0.019	0.068
	2QU2	0.041	0.029	0.162
	Mean	0.038	0.015	0.009*
2Q11+1W51	2Q11	0.010	0.018	0.586
	1W51	0.108	0.033	0.001*
	Mean	0.059	0.016	0.000*
1XS7+1W51	1XS7	-0.010	0.012	0.388
	1W51	0.062	0.021	0.002*
	Mean	0.026	0.009	0.003*
1SGZ+1W51	1SGZ	0.041	0.028	0.141
	1W51	0.105	0.026	0.000*
	Mean	0.073	0.013	0.000*
1M4H+1W51	1M4H	-0.034	0.009	0.000*
	1W51	0.030	0.014	0.029*
	Mean	-0.002	0.007	0.797
2VA7+1W51	2VA7	-0.030	0.023	0.190
	1W51	0.022	0.013	0.092
	Mean	-0.004	0.012	0.733
2IQG+1W51	2IQG	-0.016	0.014	0.255
	1W51	0.037	0.015	0.011*
	Mean	0.011	0.007	0.139
2VJ7+1W51	2VJ7	0.015	0.017	0.366
	1W51	0.063	0.026	0.015*
	Mean	0.039	0.012	0.001*
2QU2+1W51	2QU2	0.036	0.033	0.286
	1W51	0.082	0.027	0.002*
	Mean	0.059	0.017	0.001*
3E3W+1W51	3E3W	-0.013	0.018	0.466
	1W51	0.026	0.017	0.114
	Mean	0.007	0.010	0.481
1YM4+1W51	1YM4	0.002	0.013	0.853
	1W51	0.041	0.016	0.009*
	Mean	0.022	0.008	0.008*
1FKN+1W51	1FKN	-0.001	0.017	0.929
	1W51	0.033	0.013	0.012*
	Mean	0.016	0.008	0.052

2QP8+1W51	2QP8	0.010	0.018	0.575
	1W51	0.032	0.015	0.033*
	Mean	0.021	0.009	0.023*
1W50+1W51	1W50	-0.015	0.021	0.484
	1W51	-0.006	0.002	0.006*
	Mean	-0.010	0.011	0.340
2Q11+1XS7	2Q11	0.014	0.016	0.402
	1XS7	0.040	0.027	0.143
	Mean	0.027	0.013	0.041*
2Q11+1SGZ	2Q11	0.015	0.013	0.265
	1SGZ	0.049	0.032	0.118
	Mean	0.032	0.014	0.026*
2Q11+1M4H	2Q11	0.025	0.017	0.145
	1M4H	0.060	0.027	0.026*
	Mean	0.042	0.013	0.001*
2Q11+2VA7	2Q11	0.006	0.010	0.539
	2VA7	0.052	0.035	0.145
	Mean	0.029	0.018	0.101
2Q11+2IQG	2Q11	0.001	0.011	0.964
	2IQG	0.046	0.026	0.078
	Mean	0.023	0.012	0.046*
2Q11+2VJ7	2Q11	-0.023	0.015	0.111
	2VJ7	0.027	0.021	0.210
	Mean	0.002	0.010	0.867
2Q11+2QU2	2Q11	0.011	0.007	0.139
	2QU2	0.062	0.034	0.068
	Mean	0.036	0.016	0.023*
2Q11+3E3W	2Q11	0.025	0.016	0.101
	3E3W	0.085	0.035	0.015*
	Mean	0.055	0.017	0.001*
2Q11+1YM4	2Q11	-0.007	0.017	0.670
	1YM4	0.053	0.024	0.029*
	Mean	0.023	0.012	0.052
2Q11+1FKN	2Q11	0.004	0.010	0.721
	1FKN	0.068	0.032	0.036*
	Mean	0.036	0.016	0.022*
2Q11+2QP8	2Q11	-0.019	0.012	0.129
	2QP8	0.058	0.025	0.021*
	Mean	0.019	0.011	0.075
2Q11+1W50	2Q11	0.000	0.000	0.633
	1W50	0.089	0.037	0.016*
	Mean	0.045	0.019	0.016*
2Q11+1W51	2Q11	0.010	0.018	0.586
	1W51	0.108	0.033	0.001*
	Mean	0.059	0.016	0.000*
2VA7+2QU2	2VA7	0.055	0.035	0.110
	2QU2	0.061	0.020	0.002*

	Mean	0.058	0.017	0.001*
1YM4+2QU2	1YM4	0.059	0.022	0.007*
	2QU2	0.051	0.034	0.134
	Mean	0.055	0.015	0.000*
2QU2+1SGZ	2QU2	0.029	0.024	0.214
	1SGZ	0.012	0.014	0.387
	Mean	0.021	0.012	0.079
1XS7+2QU2+1SGZ	1XS7	0.069	0.026	0.008*
	2QU2	0.094	0.030	0.002*
	1SGZ	0.077	0.025	0.002*
	Mean	0.080	0.015	0.000*
3E3W+2QU2+1SGZ	3E3W	0.073	0.034	0.031*
	2QU2	0.065	0.025	0.008*
	1SGZ	0.048	0.019	0.013*
	Mean	0.062	0.015	0.000*
1M4H+2QU2+1SGZ	1M4H	0.081	0.024	0.001*
	2QU2	0.098	0.032	0.002*
	1SGZ	0.081	0.029	0.005*
	Mean	0.087	0.017	0.000*
2Q11+2QU2+1SGZ	2Q11	0.018	0.013	0.163
	2QU2	0.070	0.032	0.027*
	1SGZ	0.053	0.032	0.094
	Mean	0.047	0.017	0.006*

Table S5: The AUC metric, AUC standard error estimate (SE; calculated using Eq.(6)), Mean GlideScore (MGS), and ensemble construction strategy (see Table 5) for the cAbl ensembles. The MGS metric is simply the mean docking score (GlideScore) of the top 1% of compounds in the ranked list [Rao *et al*, J. Comput.-Aided Mol. Des. (2008), **22**, 621-627].

Ensemble	AUC	SE	MGS	Construction Strategy
3CS9+2HYY	0.899	0.015	-11.794	A
3CS9+1IEP	0.901	0.015	-11.933	A
1M52+2HZI	0.884	0.016	-11.629	A
1M52+2G2H	0.878	0.016	-10.252	A
2QOH+2G2H	0.918	0.013	-10.832	A
2HZ0+2G2F	0.891	0.016	-11.634	A
2G2F+2G1T	0.771	0.021	-8.492	A
2HIW+1FPU	0.878	0.016	-11.457	A
3CS9+1M52	0.908	0.014	-11.719	B
3CS9+2HZ0	0.898	0.015	-11.912	B
3CS9+2HIW	0.904	0.014	-11.955	B
3CS9+2GQG	0.919	0.013	-11.658	B
1M52+2HZ0	0.879	0.016	-11.698	B
1M52+2HIW	0.898	0.015	-11.452	B
1M52+2GQG	0.895	0.014	-10.410	B
2HZ0+2HIW	0.884	0.016	-12.111	B
2HZ0+2GQG	0.902	0.014	-11.634	B
3CS9+2QOH	0.921	0.013	-11.693	B
2QOH+2HZ0	0.913	0.014	-11.694	B
2QOH+2HIW	0.932	0.011	-11.562	B
2QOH+2GQG	0.930	0.012	-10.844	B
2QOH+2G2F	0.924	0.013	-10.832	C
3CS9+2G2F	0.916	0.013	-11.658	C
2HYY+2G2F	0.903	0.015	-10.956	C
2GQG+2G2F	0.893	0.014	-9.979	C
2HIW+2G2F	0.895	0.015	-11.282	C
1IEP+2G2F	0.889	0.016	-11.116	C
1FPU+2G2F	0.889	0.015	-10.823	C
1M52+2G2F	0.884	0.016	-10.205	C
2HZI+2G2F	0.896	0.015	-11.626	C
2HZ0+2G2F	0.891	0.016	-11.634	C
2G2H+2G2F	0.854	0.018	-9.466	C
2QOH+3CS9	0.921	0.013	-11.693	D
2QOH+2HYY	0.926	0.012	-11.248	D
2QOH+2GQG	0.930	0.012	-10.844	D
2QOH+2HIW	0.932	0.011	-11.562	D
2QOH+1IEP	0.928	0.012	-11.367	D
2QOH+1FPU	0.919	0.013	-11.156	D
2QOH+1M52	0.912	0.013	-10.912	D
2QOH+2HZI	0.904	0.014	-11.634	D
2QOH+2HZ0	0.913	0.014	-11.694	D
2QOH+2G2H	0.918	0.013	-10.832	D

2QOH+2G2F	0.924	0.013	-10.832	D
2QOH+2G1T	0.877	0.016	-10.832	D
2QOH+2G2H	0.918	0.013	-10.832	E
3CS9+2G2H	0.903	0.015	-11.658	E
2GQG+2QOH	0.930	0.012	-10.844	E
2HIW+2HZI	0.899	0.015	-12.088	E
1IEP+2HZ0	0.892	0.015	-11.947	E
2QOH+3CS9+2G2H	0.923	0.013	-11.693	E
3CS9+2G2H+2G2F	0.918	0.012	-11.658	E

Table S6: Comparing the virtual screening performance of the cAbl ensembles to that of their individual constituent receptors: ΔAUC (Eq.9), the standard error estimate for ΔAUC (SEΔ; Eq.12), and the resulting *p*-value (Eq.13). "Mean" refers to the mean AUC of the ensemble's constituents – it is these comparisons that are used to judge whether ensembles are "better than average" (see Table 6). The *p*-values below 0.05 are marked with a star to emphasize significance at the 95% level.

Ensemble	Constituents	ΔAUC	SEΔ	p-value
3CS9+2HYY	3CS9	0.008	0.004	0.072
	2HYY	0.011	0.011	0.300
	Mean	0.010	0.005	0.068
3CS9+1IEP	3CS9	0.009	0.004	0.017*
	1IEP	0.036	0.014	0.009*
	Mean	0.023	0.007	0.001*
1M52+2HZI	1M52	0.026	0.013	0.042*
	2HZI	0.034	0.011	0.003*
	Mean	0.031	0.008	0.000*
1M52+2G2H	1M52	0.019	0.016	0.235
	2G2H	0.050	0.013	0.000*
	Mean	0.035	0.009	0.000*
2QOH+2G2H	2QOH	0.008	0.006	0.192
	2G2H	0.090	0.017	0.000*
	Mean	0.049	0.008	0.000*
2HZ0+2G2F	2HZ0	0.091	0.010	0.000*
	2G2F	0.069	0.021	0.001*
	Mean	0.093	0.013	0.000*
2G2F+2G1T	2G2F	-0.051	0.016	0.001*
	2G1T	0.100	0.020	0.000*
	Mean	0.024	0.012	0.039*
2HIW+1FPU	2HIW	0.009	0.009	0.314
	1FPU	0.013	0.008	0.125
	Mean	0.011	0.005	0.033*
3CS9+1M52	3CS9	0.011	0.005	0.040*
	1M52	0.052	0.018	0.004*
	Mean	0.032	0.009	0.000*
3CS9+2HZ0	3CS9	0.001	0.006	0.849
	2HZ0	0.087	0.014	0.000*
	Mean	0.047	0.007	0.000*
3CS9+2HIW	3CS9	0.013	0.005	0.008*
	2HIW	0.035	0.014	0.010*
	Mean	0.024	0.007	0.000*
3CS9+2GQG	3CS9	0.025	0.010	0.009*
	2GQG	0.037	0.014	0.006*
	Mean	0.032	0.007	0.000*
1M52+2HZ0	1M52	0.021	0.016	0.187
	2HZ0	0.071	0.008	0.000*
	Mean	0.052	0.009	0.000*

1M52+2HIW	1M52	0.047	0.013	0.001*
	2HIW	0.029	0.012	0.014*
	Mean	0.038	0.008	0.000*
1M52+2GQG	1M52	0.042	0.017	0.015*
	2GQG	0.013	0.007	0.059
	Mean	0.028	0.008	0.001*
2HZ0+2HIW	2HZ0	0.085	0.010	0.000*
	2HIW	0.015	0.012	0.218
	Mean	0.055	0.008	0.000*
2HZ0+2GQG	2HZ0	0.090	0.012	0.000*
	2GQG	0.020	0.013	0.124
	Mean	0.060	0.010	0.000*
3CS9+2QOH	3CS9	0.025	0.008	0.002*
	2QOH	0.014	0.009	0.145
	Mean	0.020	0.005	0.000*
2QOH+2HZ0	2QOH	0.002	0.008	0.777
	2HZ0	0.101	0.013	0.000*
	Mean	0.055	0.007	0.000*
2QOH+2HIW	2QOH	0.024	0.007	0.001*
	2HIW	0.064	0.016	0.000*
	Mean	0.045	0.008	0.000*
2QOH+2GQG	2QOH	0.023	0.010	0.023*
	2GQG	0.048	0.012	0.000*
	Mean	0.036	0.007	0.000*
2QOH+2G2F	2QOH	0.019	0.006	0.001*
	2G2F	0.102	0.021	0.000*
	Mean	0.061	0.011	0.000*
3CS9+2G2F	3CS9	0.025	0.007	0.000*
	2G2F	0.094	0.021	0.000*
	Mean	0.060	0.010	0.000*
2HYY+2G2F	2HYY	0.016	0.007	0.029*
	2G2F	0.082	0.021	0.000*
	Mean	0.049	0.010	0.000*
2GQG+2G2F	2GQG	0.011	0.018	0.536
	2G2F	0.071	0.021	0.001*
	Mean	0.041	0.010	0.000*
2HIW+2G2F	2HIW	0.027	0.011	0.017*
	2G2F	0.074	0.020	0.000*
	Mean	0.050	0.010	0.000*
1IEP+2G2F	1IEP	0.027	0.015	0.082
	2G2F	0.067	0.020	0.001*
	Mean	0.047	0.010	0.000*
1FPU+2G2F	1FPU	0.024	0.009	0.009*
	2G2F	0.068	0.020	0.001*
	Mean	0.046	0.010	0.000*
1M52+2G2F	1M52	0.036	0.013	0.005*
	2G2F	0.062	0.019	0.001*
	Mean	0.050	0.011	0.000*

2HZI+2G2F	2HZI	0.052	0.013	0.000*
	2G2F	0.074	0.020	0.000*
	Mean	0.067	0.011	0.000*
2HZ0+2G2F	2HZ0	0.091	0.010	0.000*
	2G2F	0.069	0.021	0.001*
	Mean	0.093	0.013	0.000*
2G2H+2G2F	2G2H	0.031	0.011	0.004*
	2G2F	0.032	0.018	0.073
	Mean	0.032	0.009	0.001*
2QOH+3CS9	2QOH	0.014	0.009	0.145
	3CS9	0.025	0.008	0.002*
	Mean	0.020	0.005	0.000*
2QOH+2HYY	2QOH	0.020	0.008	0.012*
	2HYY	0.038	0.013	0.004*
	Mean	0.029	0.006	0.000*
2QOH+2GQG	2QOH	0.023	0.010	0.023*
	2GQG	0.048	0.012	0.000*
	Mean	0.036	0.007	0.000*
2QOH+2HIW	2QOH	0.024	0.007	0.001*
	2HIW	0.064	0.016	0.000*
	Mean	0.045	0.008	0.000*
2QOH+1IEP	2QOH	0.018	0.007	0.016*
	1IEP	0.061	0.015	0.000*
	Mean	0.040	0.007	0.000*
2QOH+1FPU	2QOH	0.012	0.007	0.090
	1FPU	0.052	0.014	0.000*
	Mean	0.033	0.007	0.000*
2QOH+1M52	2QOH	0.002	0.004	0.650
	1M52	0.054	0.017	0.001*
	Mean	0.028	0.008	0.001*
2QOH+2HZI	2QOH	-0.006	0.006	0.239
	2HZI	0.051	0.016	0.001*
	Mean	0.023	0.008	0.004*
2QOH+2HZ0	2QOH	0.002	0.008	0.777
	2HZ0	0.101	0.013	0.000*
	Mean	0.055	0.007	0.000*
2QOH+2G2H	2QOH	0.008	0.006	0.192
	2G2H	0.090	0.017	0.000*
	Mean	0.049	0.008	0.000*
2QOH+2G2F	2QOH	0.019	0.006	0.001*
	2G2F	0.102	0.021	0.000*
	Mean	0.061	0.011	0.000*
2QOH+2G1T	2QOH	-0.030	0.008	0.001*
	2G1T	0.206	0.024	0.000*
	Mean	0.090	0.013	0.000*

2QOH+2G2H	2QOH	0.008	0.006	0.192
	2G2H	0.090	0.017	0.000*
	Mean	0.049	0.008	0.000*
3CS9+2G2H	3CS9	0.006	0.006	0.306
	2G2H	0.078	0.018	0.000*
	Mean	0.043	0.009	0.000*
2GQG+2QOH	2GQG	0.048	0.012	0.000*
	2QOH	0.023	0.010	0.023*
	Mean	0.036	0.007	0.000*
2HIW+2HZI	2HIW	0.030	0.013	0.019*
	2HZI	0.052	0.013	0.000*
	Mean	0.043	0.008	0.000*
1IEP+2HZ0	1IEP	0.025	0.013	0.046*
	2HZ0	0.087	0.011	0.000*
	Mean	0.062	0.008	0.000*
2QOH+3CS9+2G2H	2QOH	0.016	0.010	0.102
	3CS9	0.027	0.008	0.001*
	2G2H	0.099	0.019	0.000*
	Mean	0.049	0.008	0.000*
3CS9+2G2H+2G2F	3CS9	0.022	0.007	0.003*
	2G2H	0.094	0.018	0.000*
	2G2F	0.097	0.022	0.000*
	Mean	0.070	0.011	0.000*

Table S7: Numbers of successful ensembles for each construction strategy: as Table 6 in the main text, except that ΔAUC has been determined using Eq.(7) rather than Eq.(9).

Protein	Construction Strategy	Total	Better than all	Better than average
BACE	A	13	1	5
	B	6	1	5
	C	13	0	7
	D	13	0	9
	E	7	3	6
cAbl	A	8	2	7
	B	13	4	13
	C	11	8	11
	D	12	3	12
	E	7	3	7

Table S8: As Table 7 in the main text, except that ΔAUC has been determined using Eq.(7) rather than Eq.(9).

Ensemble	AUC	PDB	AUC	ΔAUC	p-value
ensIFDa	0.824	2Q11	0.774	0.050	0.250
		1XS7	0.757	0.067	0.062
		1SGZ	0.740	0.084	0.093
		1M4H	0.748	0.076	0.014*
		2VA7	0.730	0.094	0.002*
		2IQG	0.732	0.092	0.014*
		2VJ7	0.742	0.082	0.054
		2QU2	0.717	0.107	0.058
		3E3W	0.714	0.110	0.000*
		1YM4	0.725	0.099	0.001*
		1FKN	0.723	0.101	0.004*
		2QP8	0.697	0.126	0.002*
		1W50	0.686	0.138	0.000*
		1W51	0.688	0.135	0.000*
		ensIFDaag	0.734	0.090	0.002*
		ensIFDaap	0.696	0.128	0.000*
		ensIFDahe	0.760	0.064	0.013*
		ensIFDahea	0.780	0.043	0.130
		ensIFDain	0.753	0.071	0.036*
		ensIFDaip	0.716	0.108	0.002*
		ensIFDara	0.755	0.069	0.004*

Table S9: As Table 8 in the main text, except that ΔAUC has been determined using Eq.(7) rather than Eq.(9).

Ensemble	AUC	PDB	AUC	ΔAUC	p-value
ensIFDc	0.937	2QOH	0.911	0.026	0.019*
		3CS9	0.895	0.042	0.002*
		2HYY	0.885	0.051	0.001*
		2GQG	0.884	0.052	0.001*
		2HIW	0.866	0.071	0.000*
		1IEP	0.868	0.069	0.000*
		1FPU	0.867	0.070	0.000*
		1M52	0.860	0.077	0.000*
		2HZI	0.854	0.083	0.000*
		2HZ0	0.834	0.103	0.000*
		2G2H	0.831	0.106	0.000*
		2G2F	0.823	0.114	0.000*
		2G1T	0.670	0.267	0.000*
		ensIFDc1	0.924	0.013	0.127
		ensIFDc2	0.903	0.034	0.015*
		ensIFDc6	0.886	0.051	0.000*
		ensIFDc8	0.871	0.066	0.000*
		ensIFDc11	0.923	0.014	0.172
		ensIFDc17	0.900	0.036	0.000*
		ensIFDc18	0.871	0.066	0.000*

Table S10: BACE ensemble ensIFDb constructed using the Induced-Fit Docking (IFD) approach with receptor 2Q11 as the initial structure: *p*-values for differences in the AUC values of the ensemble, the crystallographically-derived single receptors, and the constituent IFD-derived single receptors. The *p*-values are two-sided for H_1: ΔAUC not equal to 0, where ΔAUC is determined using Eq.(9) rather than Eq.(7). The *p*-values below 0.05 are marked with a star to emphasize significance at the 95% level. The reference (i.e. ``training'') compounds used in the IFD protocol were excluded from the analyses used to produce all the values in this table. The constituent IFD-derived single receptors are labelled ensIFDb*x*, where *x* indicates the chemotype used to prepare the receptor (ag=acylguanidine, ap=arylpiperazine, he=hydroxyethyl, hea=hydroxyethylamine, in=isonicotinamide, ip=isophthalamide, ra=reduced amide).

Ensemble	**AUC**	**PDB**	**AUC**	**ΔAUC**	***p*-value**
ensIFDb	0.836	2Q11	0.774	0.063	0.058
		1XS7	0.757	0.079	0.065
		1SGZ	0.740	0.096	0.000*
		1M4H	0.748	0.089	0.063
		2VA7	0.730	0.106	0.014*
		2IQG	0.732	0.104	0.014*
		2VJ7	0.742	0.094	0.023*
		2QU2	0.717	0.120	0.000*
		3E3W	0.714	0.122	0.006*
		1YM4	0.725	0.111	0.022*
		1FKN	0.723	0.113	0.017*
		2QP8	0.697	0.139	0.002*
		1W50	0.686	0.151	0.001*
		1W51	0.688	0.148	0.007*
		ensIFDbag	0.785	0.051	0.066
		ensIFDbap	0.764	0.072	0.014*
		ensIFDbhe	0.714	0.123	0.000*
		ensIFDbhea	0.775	0.061	0.007*
		ensIFDbin	0.738	0.099	0.004*
		ensIFDbip	0.813	0.023	0.420
		ensIFDbra	0.770	0.066	0.050*

Table S11: Side-chain torsion angles (C-C_α-C_β-C_γ) for five important and/or highly flexible residues in the BACE active site. Measurements are shown for both the individual members of the IFD-derived ensIFDa and the fourteen crystallographic structures. All angles are measured in degrees and are wrapped to within ±180˚ of the 1W51 reference structure using the periodicity of the angular variables. Numbering as PDB structure 1FKN. The final column shows the root mean square deviation (RMSD) of each ensemble member to 1W51 in this five-dimensional torsion angle space.

Ensemble member	Ash32	Tyr71	Gln73	Asp228	Arg235	RMSD to 1W51
1W51	54	-175	78	82	176	0.0
ensIFDaag	66	-183	171	43	184	42.2
ensIFDaap	67	-305	-69	40	182	82.4
ensIFDahe	66	-188	-17	48	176	42.1
ensIFDahea	65	-187	49	61	181	16.2
ensIFDain	57	-193	178	59	179	42.8
ensIFDaip	73	-196	53	41	96	39.8
ensIFDara	64	-184	199	52	179	51.2

PDB	Ash32	Tyr71	Gln73	Asp228	Arg235	RMSD to 1W51
1W51	54	-175	78	82	176	0.0
1FKN	63	-175	170	60	176	65.4
1M4H	57	-177	57	51	192	16.7
1SGZ	53	-73	68	53	206	67.5
1W50	54	-175	129	82	180	21.1
1XS7	52	-198	53	39	176	54.6
1YM4	57	-185	43	54	188	19.7
2IQG	53	-173	45	65	198	17.7
2Q11	44	-291	-70	45	201	79.0
2QP8	55	-173	38	82	186	54.5
2QU2	68	-74	66	41	186	45.4
2VA7	54	-186	130	63	173	46.5
2VJ7	60	-179	54	63	187	58.0
3E3W	56	-74	152	55	184	52.5