Supplementary Materials

Identification of Bacterial Oligopeptidase B Inhibitors from Microbial Natural Products: Molecular Insights, Docking Studies, MD Simulations, and ADMET Predictions

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Chain A, Oligopeptidase B [Serratia proteamaculans]
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Range 1: 3 to 673

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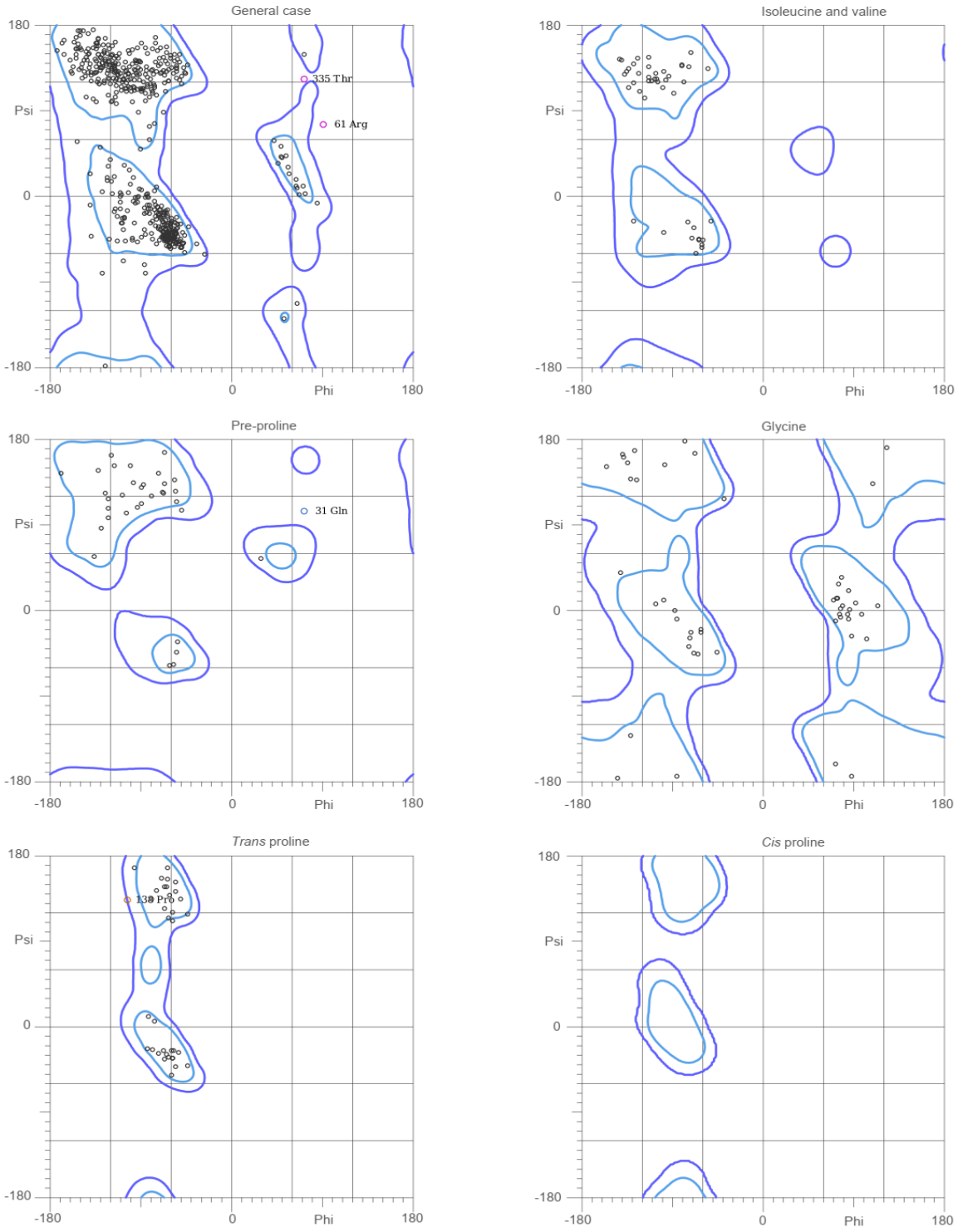
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Figure S1: Pairwise alignment of OPB sequences from *S. marcescens* and *S. proteamaculans* via BLASTp analysis

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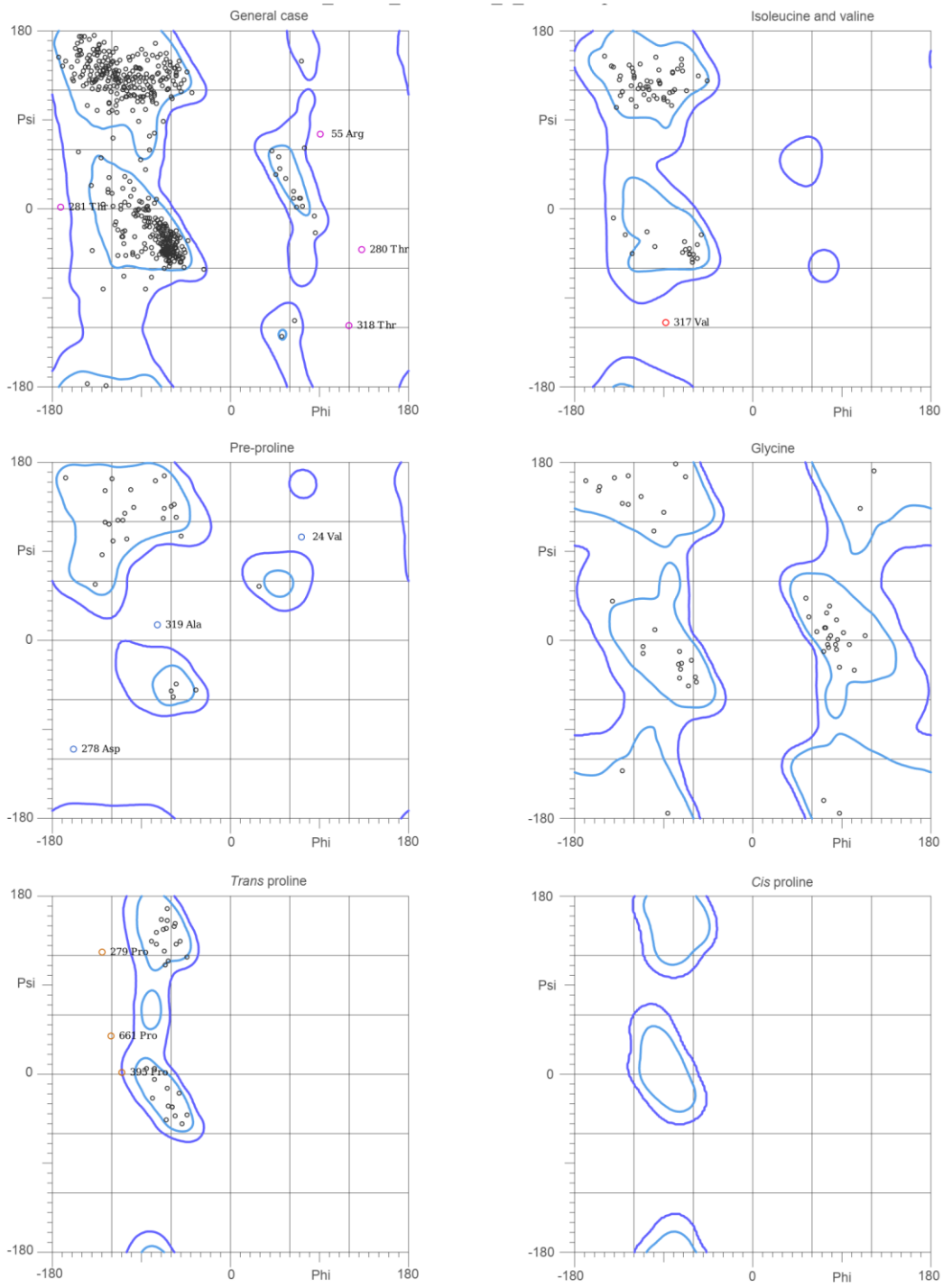


96.0% (646/673) of all residues were in favored (98%) regions.
99.4% (669/673) of all residues were in allowed (>99.8%) regions.

There were 4 outliers (phi, psi):
31 Gln (73.0, 105.3)
61 Arg (91.1, 76.3)
138 Pro (-104.0, 134.9)
335 Thr (72.0, 124.1)

(A) *Serratia marcescens* OPB

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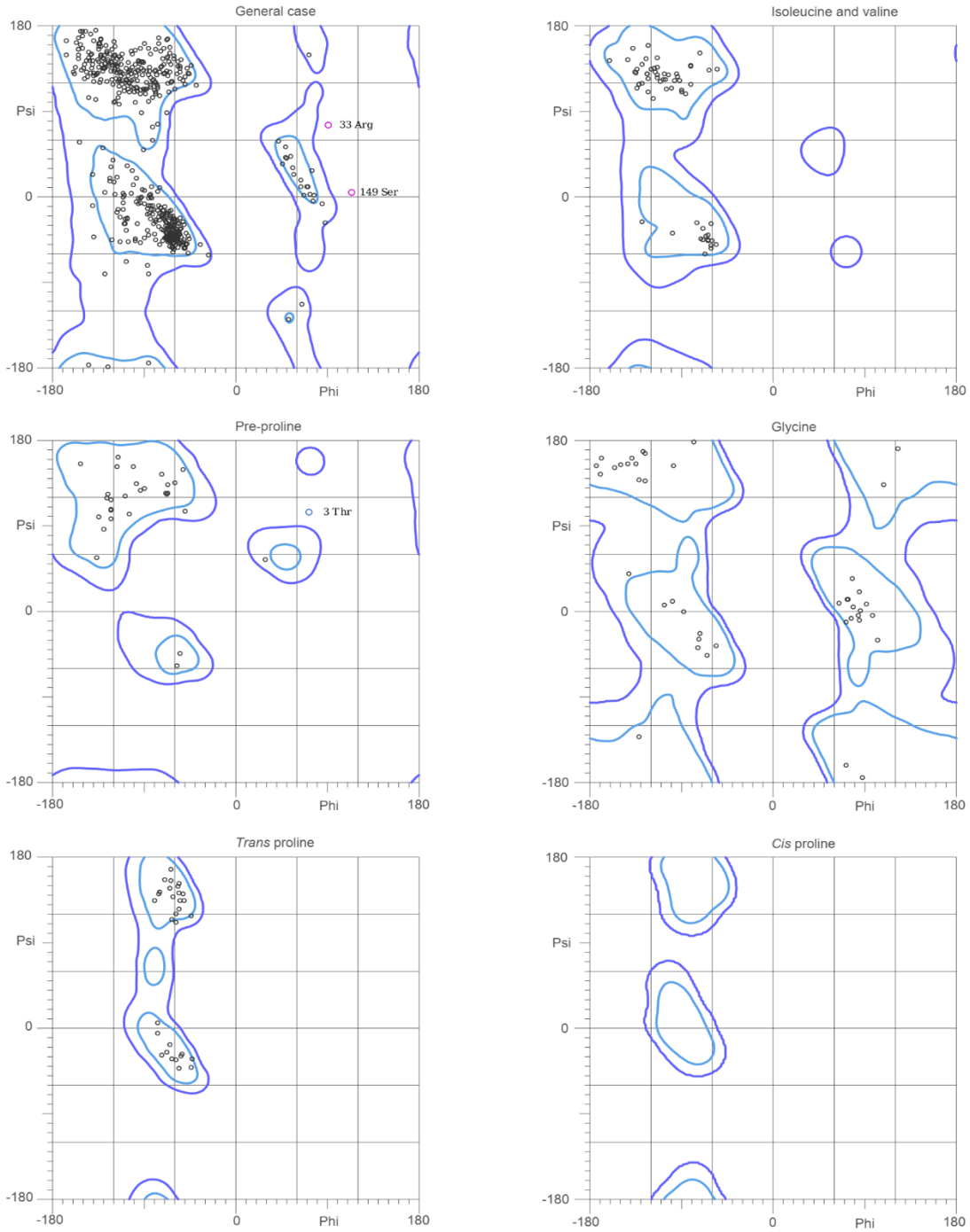
94.4% (637/675) of all residues were in favored (98%) regions.
98.4% (664/675) of all residues were in allowed (>99.8%) regions.

There were 11 outliers (phi, psi):

24 Val (73.0, 105.3)
55 Arg (91.1, 76.3)
278 Asp (-159.2, -110.9)
279 Pro (-130.6, 124.9)
280 Thr (133.4, -41.3)
281 Thr (-172.7, 3.0)
317 Val (-89.0, -115.0)
318 Thr (120.2, -118.2)
319 Ala (-74.1, 16.5)
395 Pro (-111.0, 2.7)
661 Pro (-121.0, 39.9)

(B) *Stenotrophomonas maltophilia* OPB

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96.1% (648/674) of all residues were in favored (98%) regions.
99.6% (671/674) of all residues were in allowed (>99.8%) regions.

There were 3 outliers (phi, psi):
3 Thr (73.0, 105.3)
33 Arg (91.1, 76.3)
149 Ser (114.9, 5.6)

(C) *Serratia proteamaculans* OPB

Figure S2: Ramachandran plots of OPB targets and template showing φ and ψ torsional angle distributions: (A) *Serratia marcescens*, (B) *Stenotrophomonas maltophilia*, (C) *Serratia proteamaculans*

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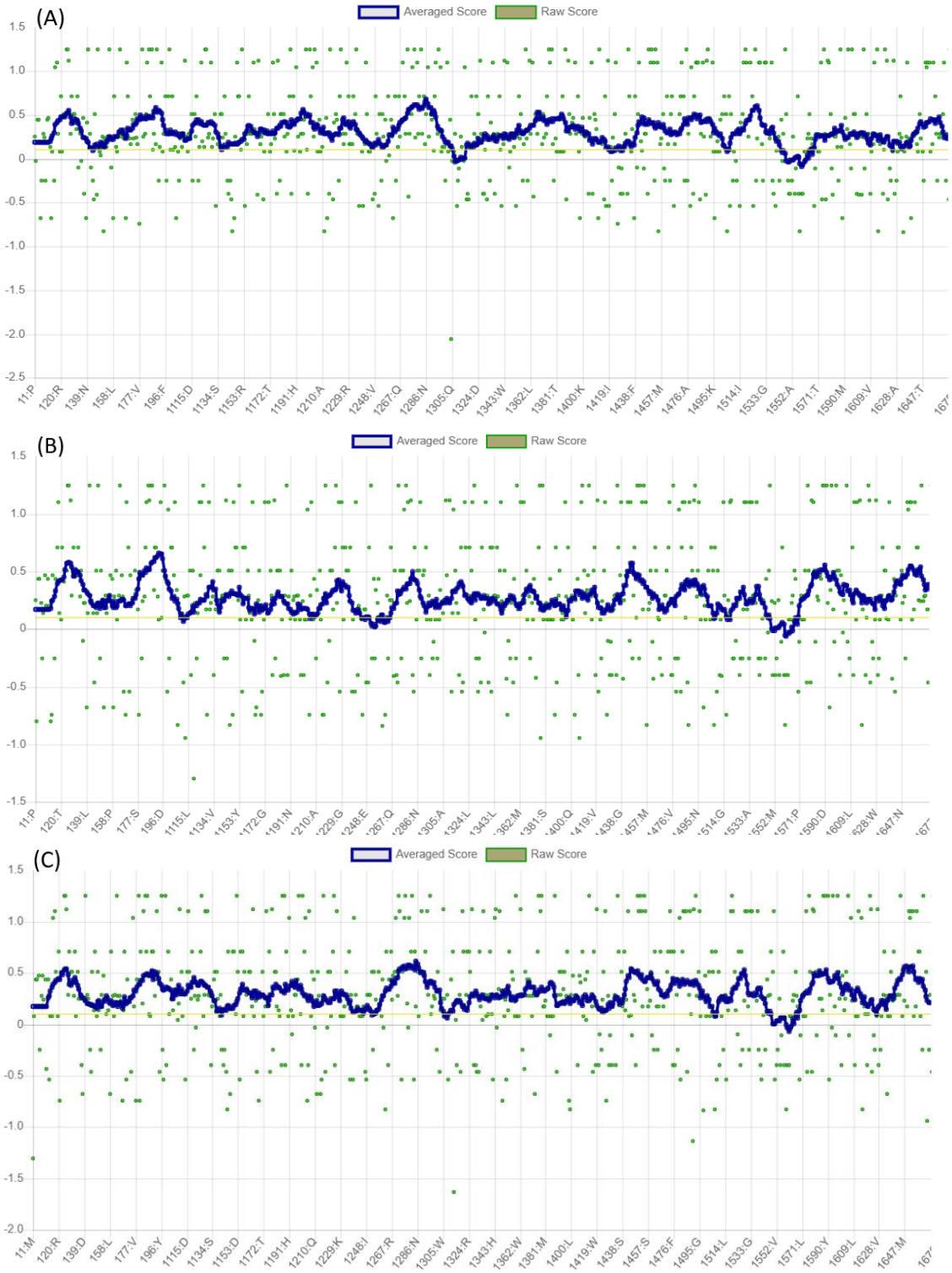


Figure S3: Verify3D structural validation profiles for OPBs, with ≥80% of residues scoring ≥0.1: (A) *S. marcescens*, (B) *S. maltophilia*, (C) *S. proteamaculans*

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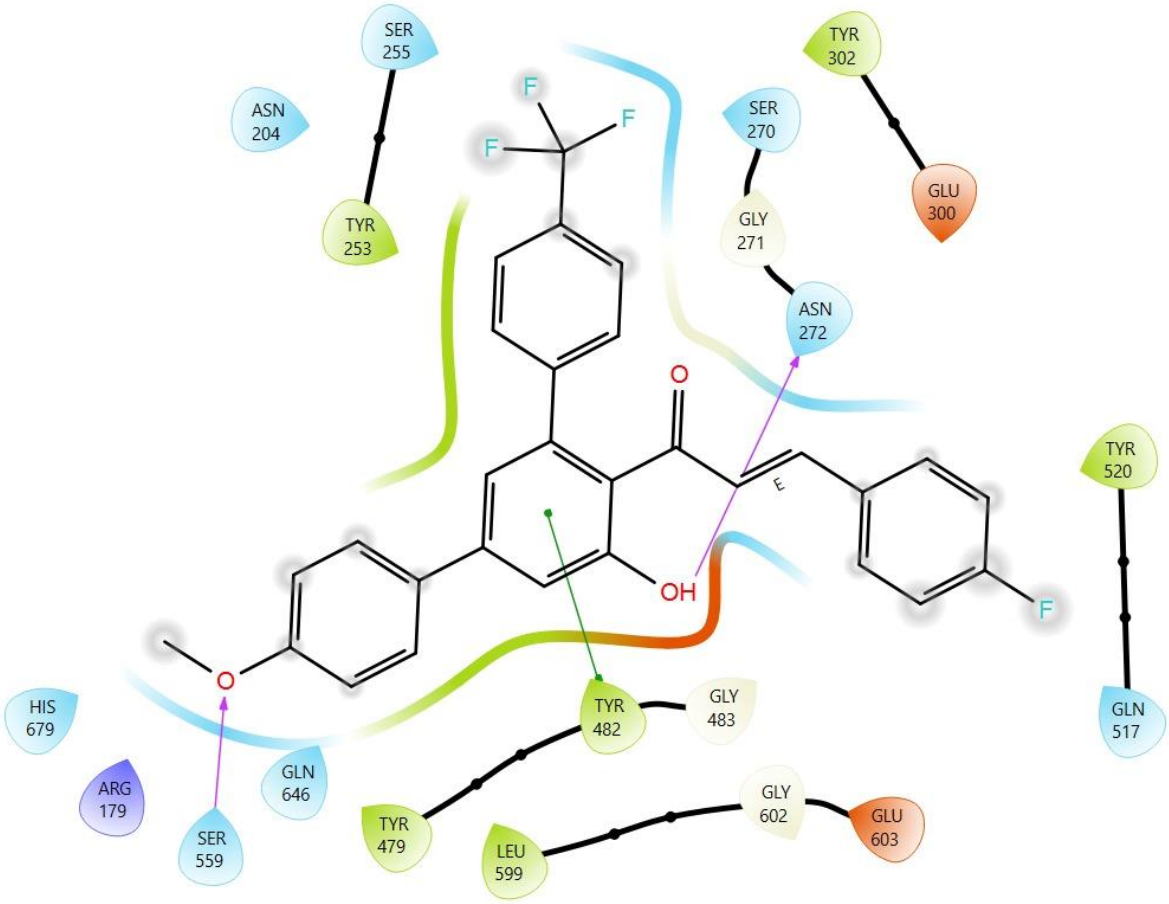
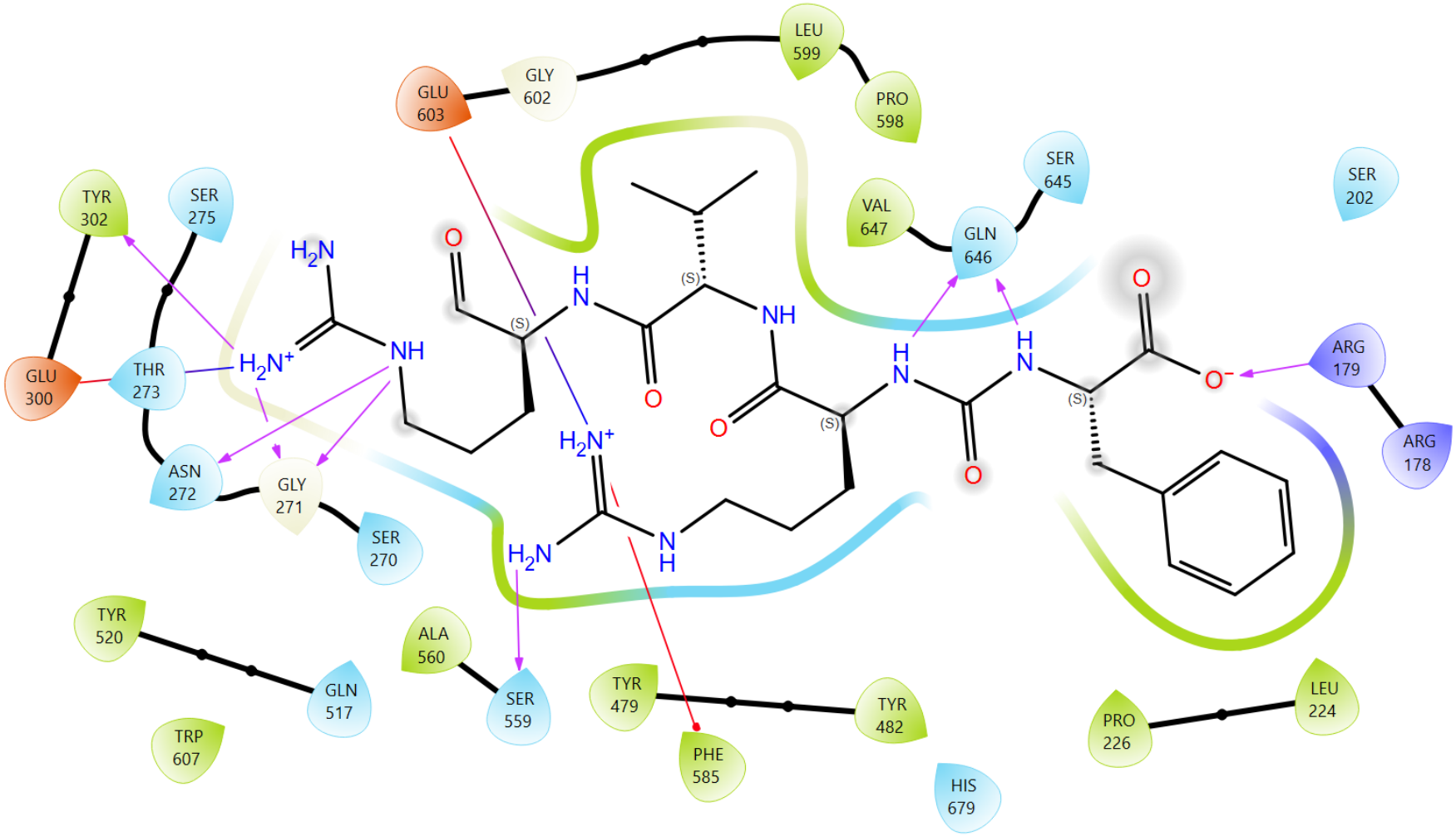


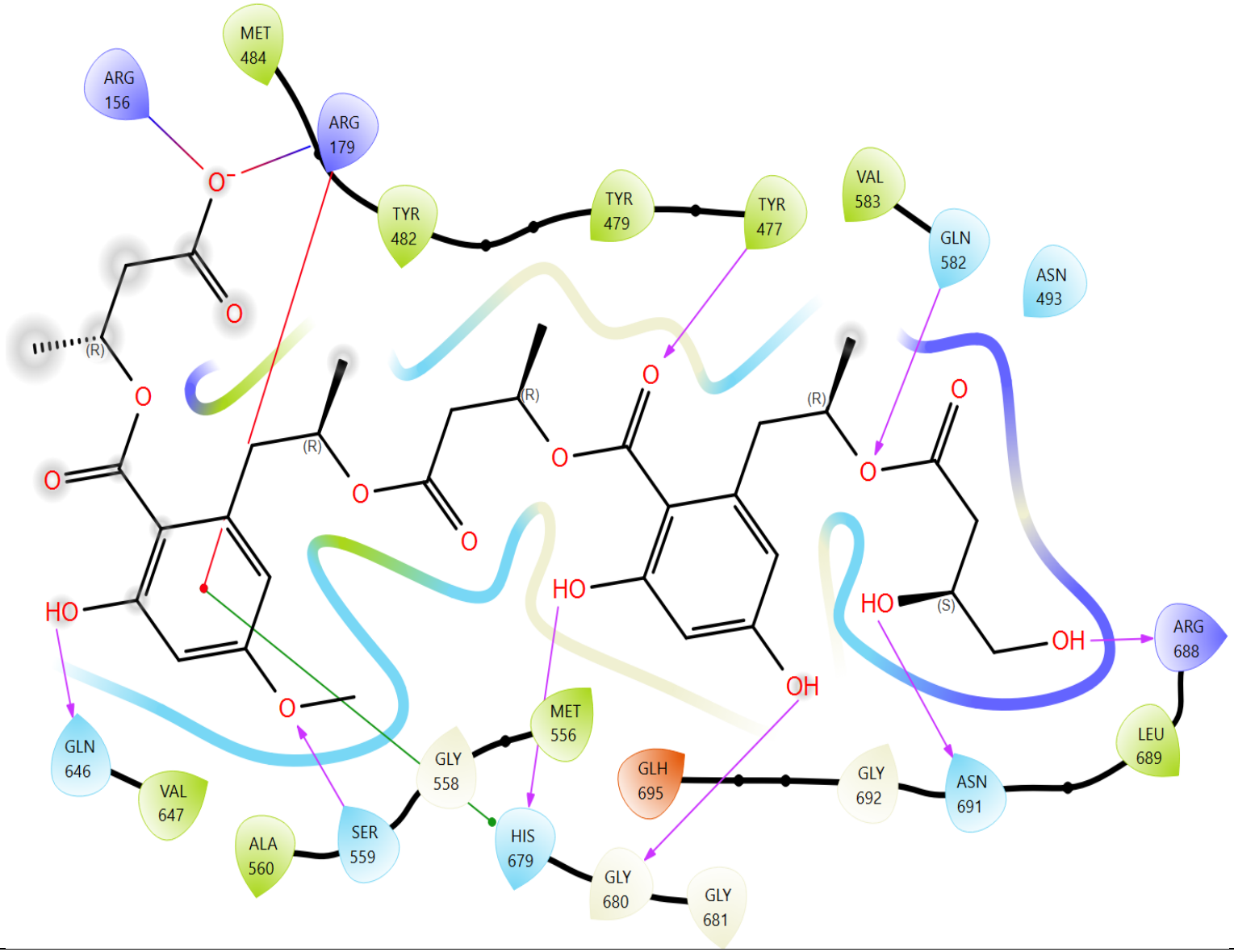
Figure S4: 2D interaction map of compound C-132 within the catalytic pocket of *Serratia marcescens* oligopeptidase B (OPB), highlighting key binding interactions.

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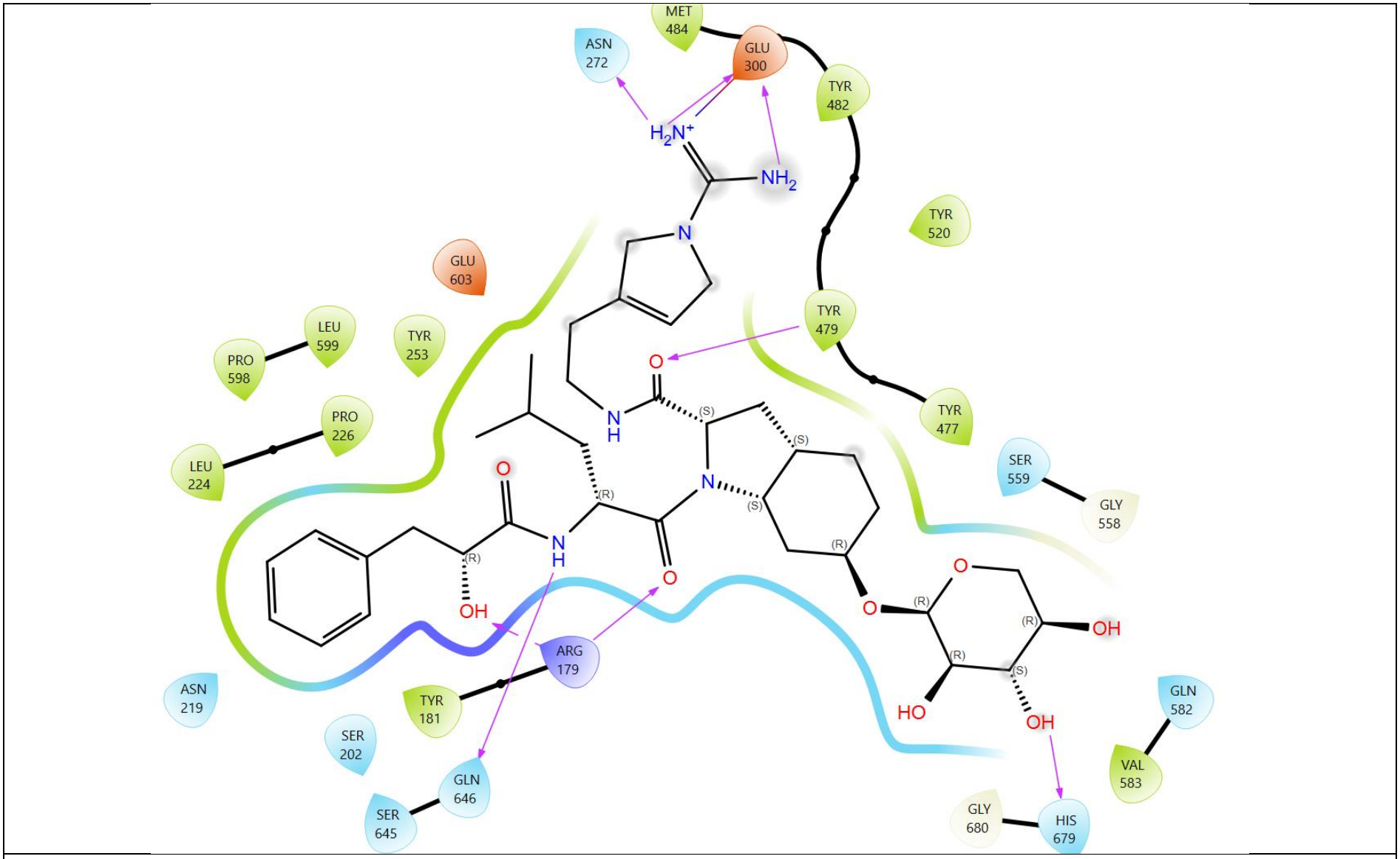
Antipain

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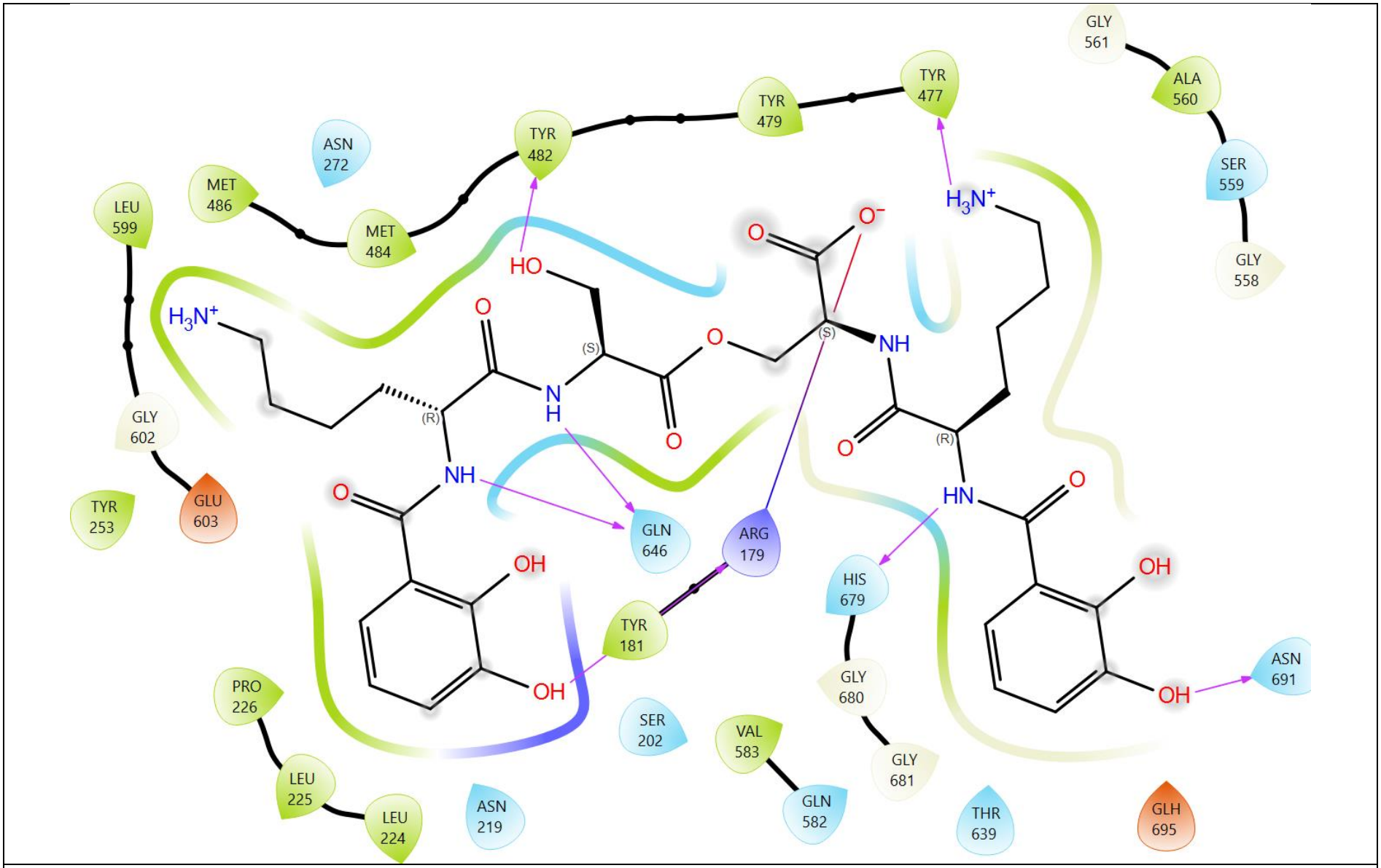
Calcaride D

Supplementary Materials



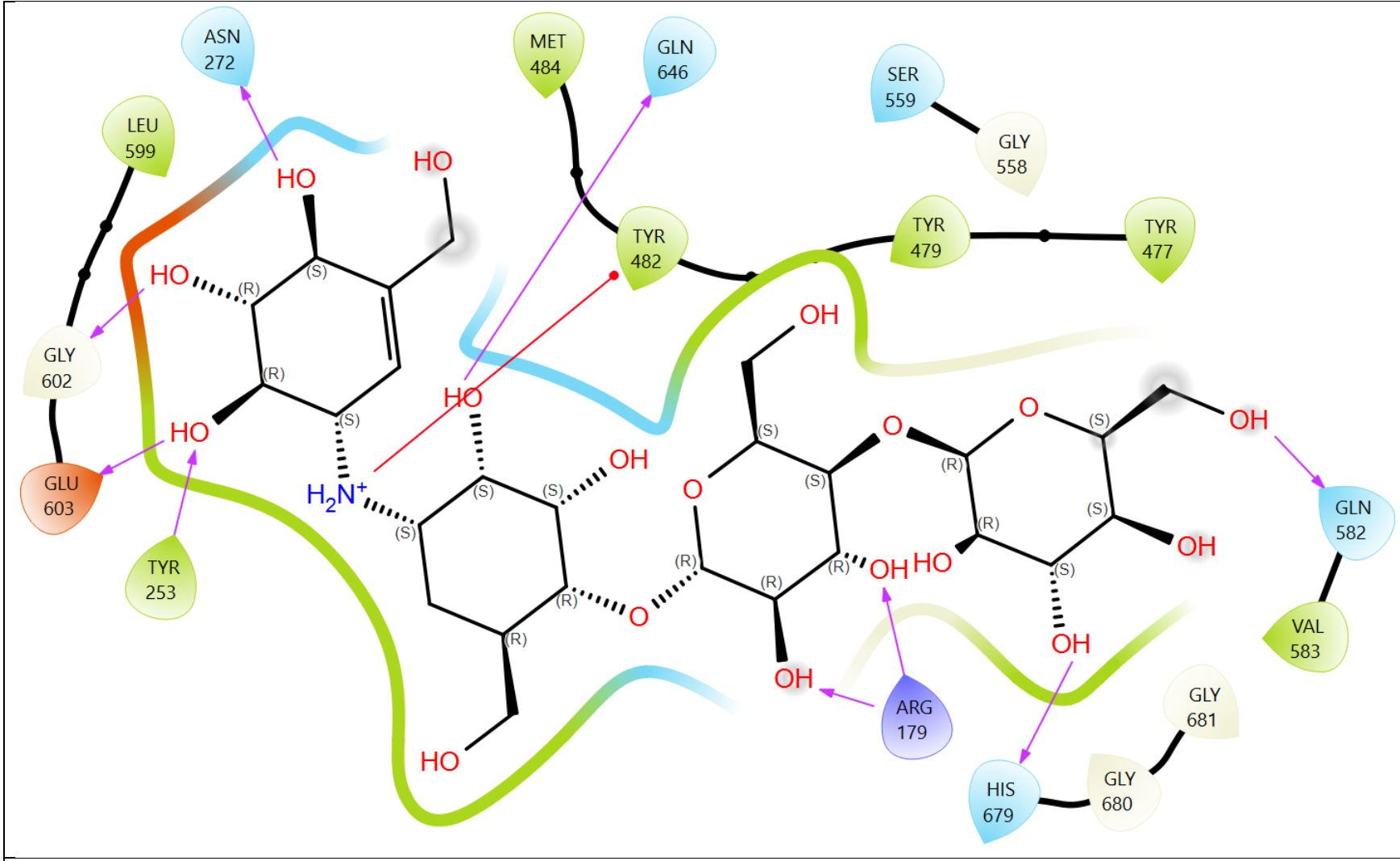
Aeruginoside 126A

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Dichrysobactin

Supplementary Materials



Validamycin E

Supplementary Materials

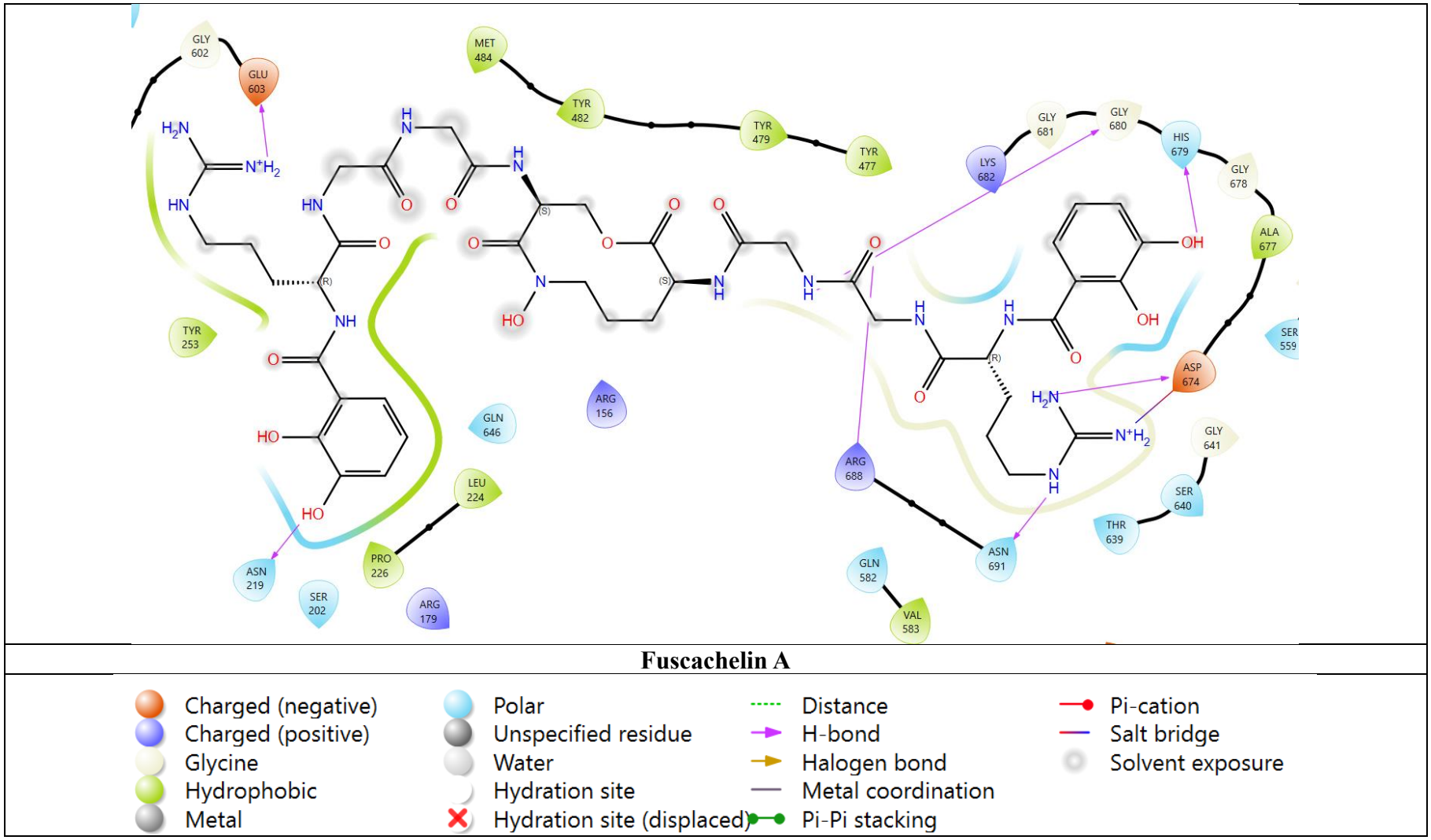


Figure S5: 2D interaction map of the top five inhibitors (Calcaride D, Aeruginoside 126A, Dichrysobactin, Validamycin E, and Fuscachelin A) along with the reference inhibitor Antipain, highlighting their binding interactions with the catalytic site of *Serratia marcescens* OPB.

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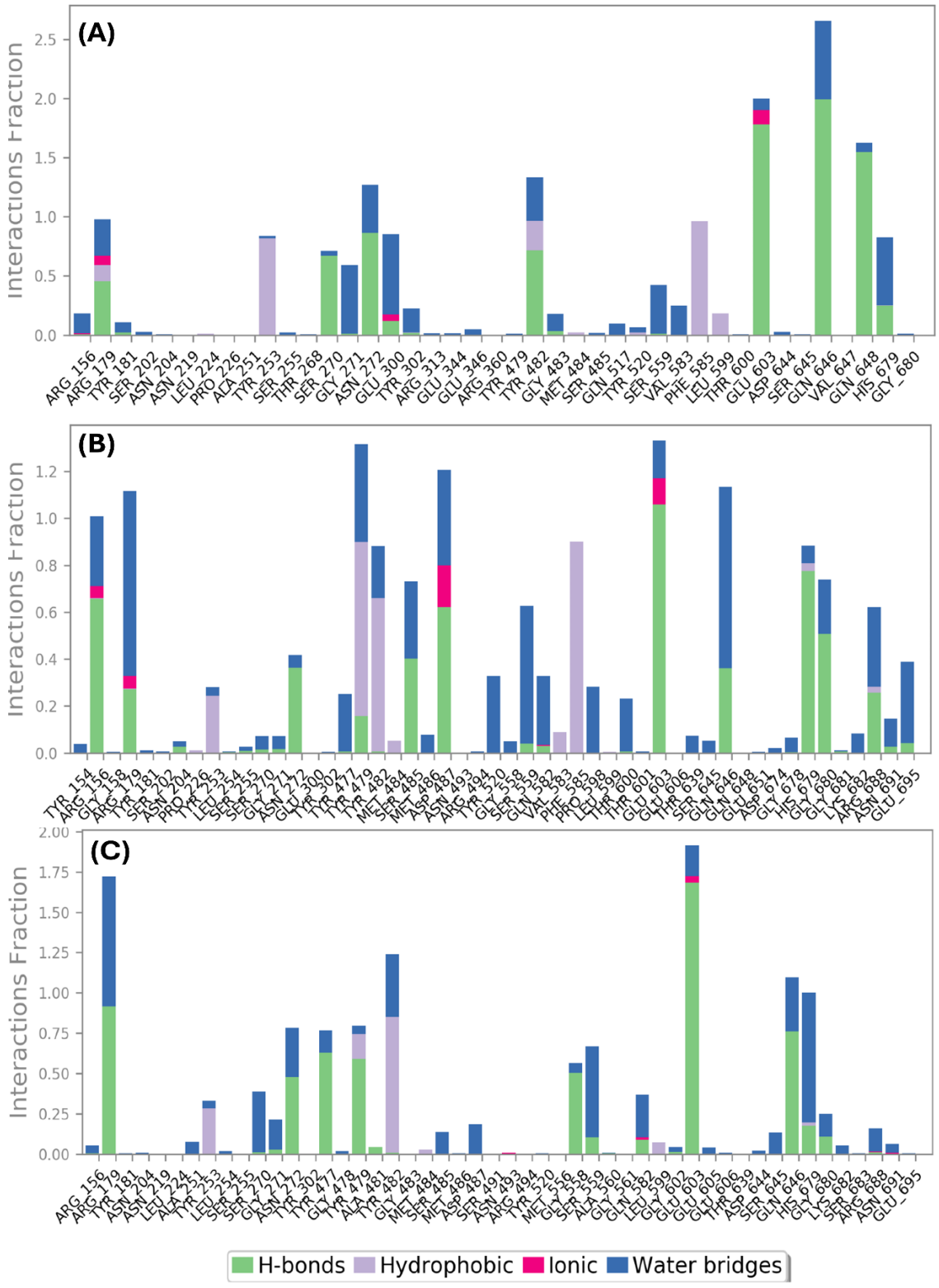


Figure S6: Histogram representation of the interactions between Antipain (A), Dichrysoisobactin (B), and Validamycin E (C) with *S. marcescens* OPB throughout the simulation run.

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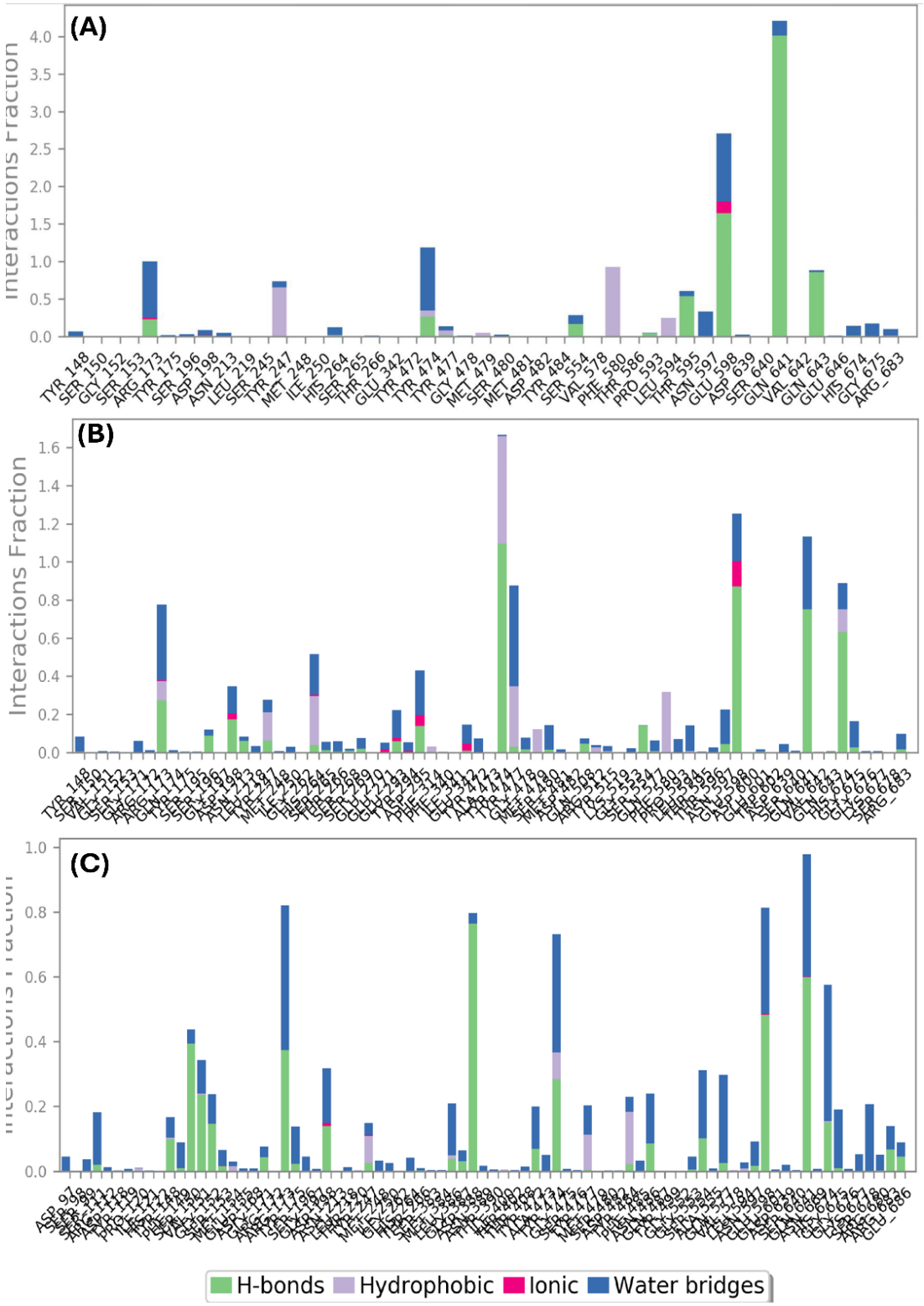


Figure S7: Histogram representation of the interactions between Antipain (A), Dichrysoisobactin (B), and Validamycin E (C) with *S. maltophilia* OPB throughout the simulation run.

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Table S1: Physicochemical and pharmacokinetics descriptors of the identified hits calculated with Qikprop

Property	Description	Permissible range	Antipain	Dichrysobactin	Validamycin E
#stars	Number of property or descriptor values that fall outside the 95% range of similar values for known drugs.	(0–5)	11	11	13
#amide	Number of non-conjugated amide groups	(0–1)	3	2	0
#rotor	Number of non-trivial, non-hindered rotatable bonds	(0–15)	21	28	24
#rtvFG	Number of reactive functional groups	(0–2)	0.00	1	2
mol_MW	Molecular weight of the molecule.	(130–725)	604.70	720.73	659.63
SASA	Total solvent accessible surface area	(300–1000)	1052.84	1150.15	885.86
FOSA	Hydrophobic component of the SASA	(0–750)	420.31	350.64	409.62
FISA	Hydrophilic component of the SASA	(7–330)	464.37	545.15	467.86
PISA	π (carbon and attached hydrogen) component of the SASA	(0–450)	168.16	254.35	8.37
WPSA	Weakly polar component of the SASA	(0–175)	0.00	0.00	0.00
donorHB	Estimated number of hydrogen bonds that would be donated by the solute to water molecules in an aqueous solution.	(0–6)	10	8	15
accptHB	Estimated number of hydrogen bonds that would be accepted by the solute from water molecules in an aqueous solution	(2–20)	12	15	32
QPlogPo/w	Predicted octanol/water partition coefficient.	(−2–6.5)	0.27	-1.95	-7.18
QPPCaco	Predicted apparent Caco-2 cell permeability in nm/sec	(<25poor, >500 great)	0.04	0.001	0.09
QPlogS	Predicted aqueous solubility	–6.5 – 0.5	-4.46	-3.25	0.92
QPlogBB	Predicted brain/blood partition coefficient.	–3.0 – 1.2	-6.80	-7.86	-5.58
QPPMDCK	Predicted apparent MDCK cell permeability in nm/sec.	<25 poor >500 great	0.03	0.00	0.02
#metab	Number of likely metabolic reactions.	(1 – 8)	9	13	15
QPlogKhsa	Prediction of binding to human serum albumin.	–1.5–1.5	-1.28	-1.06	-2.69
QPlogHERG	Predicted IC_{50} value for blockage of HERG K^+ channels.	Concern below –5	-1.05	-4.59	-5.83
Human Oral Absorption	Predicted qualitative human oral absorption	1, 2, or 3 for low, medium, or high.	1	1	1
%Human Oral Absorption	Predicted human oral absorption on 0 to 100% scale.	>80% is high	0.00	0.00	0.00
PSA	VdW surface area of polar nitrogen and oxygen atoms	7–200	313.94	357.02	299.04
Rule Of Five	Number of violations of Lipinski's rule of five	maximum is 4	3	3	3
Rule Of Three	Number of violations of Jorgensen's rule of three.	maximum is 3	2	2	2