A APPENDIX

A.1 PHYSICAL PROPERTIES PREDICTED BY FILTER

Table 2: The physical properties predicted by FILTER, along with their descriptions and expected ranges.

Physical Property	Description	Expected Range
Rule of Five	A measure of a molecule's drug-likeness based on its molecular weight, lipophilicity, and hydrogen bonding.	0-5
Ghose Filter	Evaluates drug-likeness considering molecular weight, lipophilicity, and hydrogen bonding.	0-5
MDDR-Like Rule	Assesses drug-likeness based on molecular weight, lipophilicity, and hydrogen bonding.	0-5
Rotatable Bond Count	The number of rotatable bonds in a molecule, influencing its flexibility.	0-20
Bioavailability	Extent to which a molecule is absorbed and available for use by the body.	0-100%
Number of Rings	The number of cyclic structures within a molecule, affecting its stability and binding.	0-10
H Bond Donor Count	The number of hydrogen bond donors, impacting solubility and binding interactions.	0-10
H Bond Acceptor Count	The number of hydrogen bond acceptors, influencing solubility and molecular interactions.	0-10
Physiological Charge	The net charge of a molecule at physiological pH, affecting its solubility and transport.	-10 to 10
Melting Point	The temperature at which a molecule transitions from solid to liquid.	0-500°C
Water Solubility	Degree to which a molecule dissolves in water, affecting bioavailability.	0-100%
Polar Surface Area (PSA)	Total polar surface area of a molecule, influencing membrane permeability and drug transport.	0-200 Å²
Boiling Point	The temperature at which a molecule transitions from liquid to gas.	0-500°C
logP	Measure of a molecule's lipophilicity, affecting its ability to cross cell membranes.	-10 to 10
Refractivity	Measure of a molecule's ability to refract light, related to its volume and electron distribution.	0-100
pKa (Strongest Acidic)	The pKa value of the most acidic group in a molecule, influencing its ionization state.	0-14
Polarizability	The ability of a molecule's electron cloud to be distorted by external electric fields.	0-100
pKa (Strongest Basic)	The pKa value of the most basic group in a molecule, affecting its protonation state.	0-14
pKa	General pKa value of a molecule, indicating its acid-base properties.	0-14
logS	Measure of a molecule's solubility in a solvent, impacting its bioavailability.	-10 to 10
Radioactivity	Measure of a molecule's radioactivity, important for safety and regulatory compliance.	0-100
caco2 Permeability	Assesses a molecule's permeability across the Caco-2 cell line, predicting intestinal absorption.	0-100%

A.2 RESULTS ACROSS ALL MODELS AND TARGET PROPERTIES BY FILTER

Table 3: Summary of results across all models and target properties; results in **bold** indicate the best performance for each metric.

Task Type	Target Property	Metric	NN	XGB	Combined
Binary Classification	**Bioavailability**	ROC AUC	0.9101	0.9090	**0.9104**
		Accuracy	0.8194	0.8367	**0.8367**
		Precision	**0.9700**	0.9659	0.9653
		F1 Score	0.8848	0.8974	**0.8975**
Regression	**caco2 Permeability**	RMSE	1.8883	**1.8707**	1.8583
		MAE	0.9583	**0.8674**	0.8950
Binary Classification	**Ghose Filter**	ROC AUC	0.8821	0.8810	**0.8828**
		Accuracy	0.8189	0.8166	**0.8171**
		Precision	0.8166	0.8261	**0.8246**
		F1 Score	0.8366	0.8314	**0.8323**
Regression	**logS**	RMSE	2.6052	**2.3354**	2.4140
		MAE	1.4450	**1.1462**	1.2394
Binary Classification	**MDDR-Like Rule**	ROC AUC	**0.9157**	0.9117	0.9135
		F1 Score	0.6830	0.6922	**0.6966**
Regression	**Polar Surface Area**	RMSE	0.8869	**0.8453**	0.8513
		MAE	0.5393	**0.4361**	0.4831
Regression	**pKa**	RMSE	0.5179	0.5296	**0.5184**
		MAE	**0.2335**	0.2456	0.2384
Binary Classification	**Rule of Five**	ROC AUC	0.8830	0.8792	**0.8817**
		F1 Score	0.8568	0.8606	**0.8508**

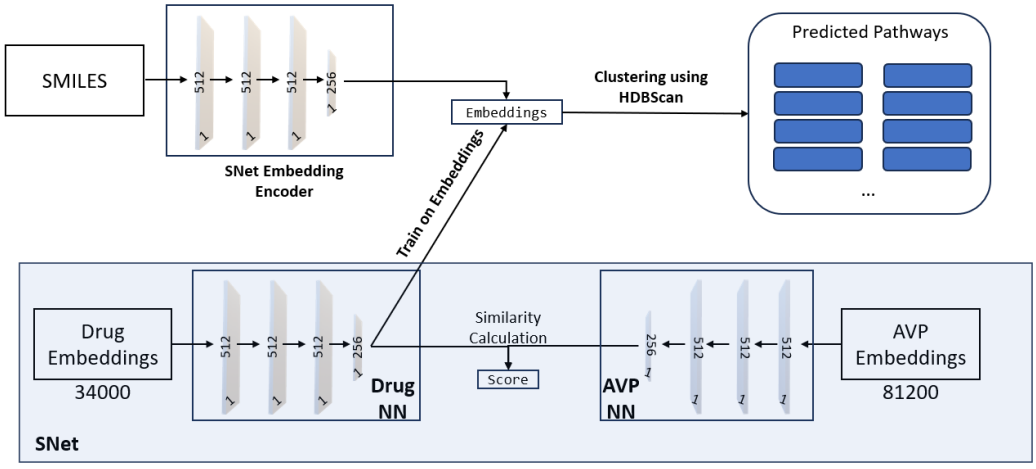

Figure 4: Prediction engine for embedding newly synthesized molecules into SNet space based on chemical structure, enabling pathway clustering and functional analysis by proximity to known drugs with established biological functions in biological space.

Table 4: Top docking scores for synthesized molecules and JNK1, JNK2, JNK3, and FA7 proteins.

SMILES	JNK1	JNK2	JNK3	FA7
C12Cc3c(c(O)ccc3)C(=O)C1=C(O)C1(O)...	13.4	11.7	13.4	9.9
C12Cc3c(c(O)ccc3N3CCN(CC3)c3ncc(F)...	12.6	11.0	12.6	6.3
C12Cc3c(c(O)ccc3n3cc(c4c3cccc4)C3...	12.4	10.8	12.4	9.4
C12Cc3c(c(O)ccc3n3c(nc(c3)CNC(=O...	12.4	14.7	12.4	10.2
C12Cc3c(c(O)ccc3n3c(ncc3c3n[nH]c4...	12.3	9.3	12.3	11.4
C12Cc3c(c(O)ccc3)C(=O)C1=C(O)C1(O...	10.0	14.5	10.0	9.7
C12Cc3c(c(O)ccc3n3cc(c4c3cccc4)C3...	9.4	13.9	9.4	7.6
n1(c(ncc1)c1nc[nH]c1c1[nH]cc(n1)C...	9.8	13.9	9.8	9.0
CCC(=C(c1ccccc1)c1ccc(cc1)ONC(=O...	9.8	10.3	13.3	7.0
CCC(=C(c1ccccc1)c1ccc(cc1)ONC(=O...	9.5	12.1	13.3	6.3
CCC(=C(c1ccccc1)c1ccc(cc1)OCCc1n...	6.5	7.3	13.3	8.0