Supplementary data

Experimental setup for screening with Non-redundant Cross-validation (NRCV)

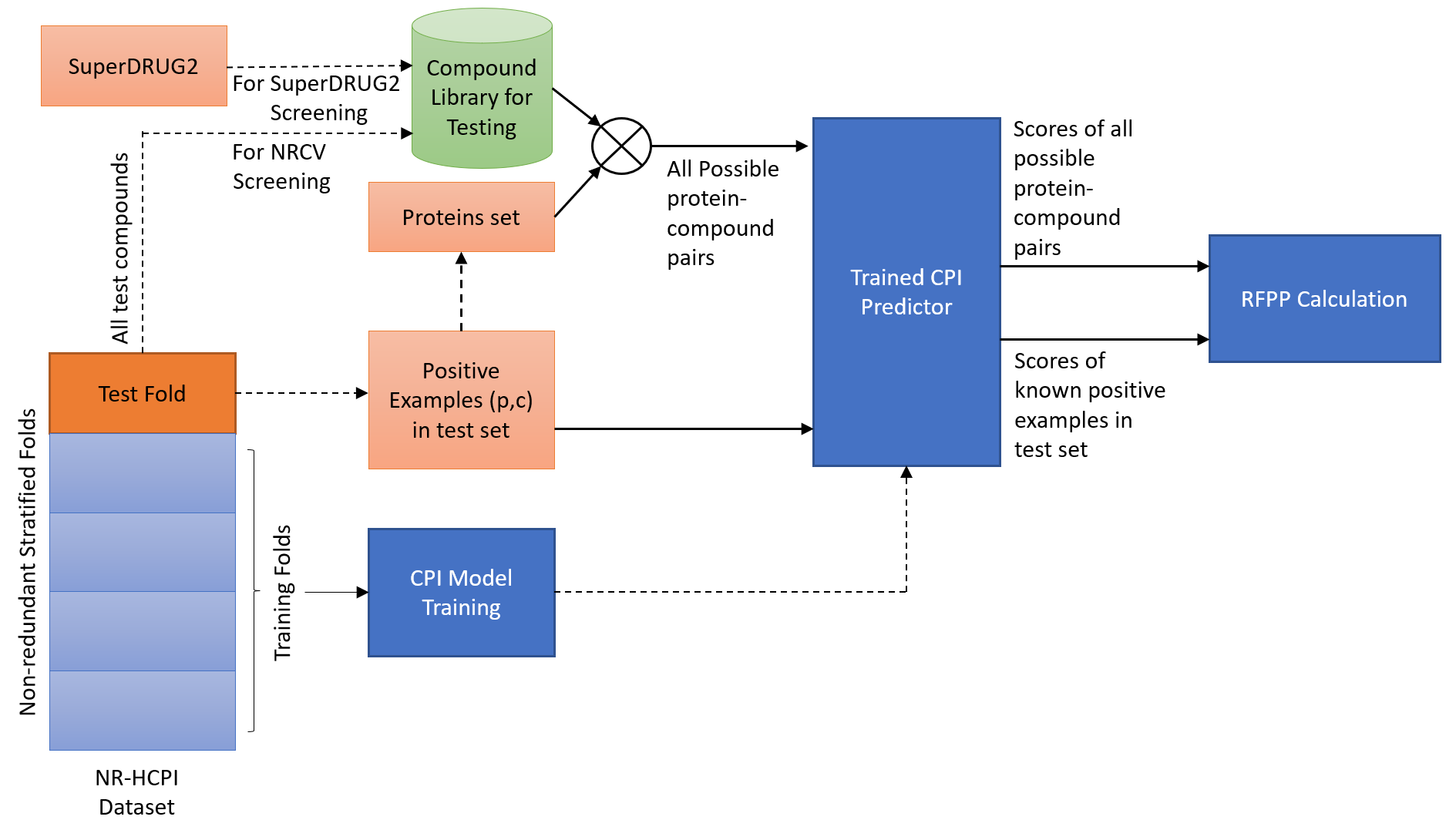


Figure 1 shows the setup of screening experiments used for RFPP calculation.

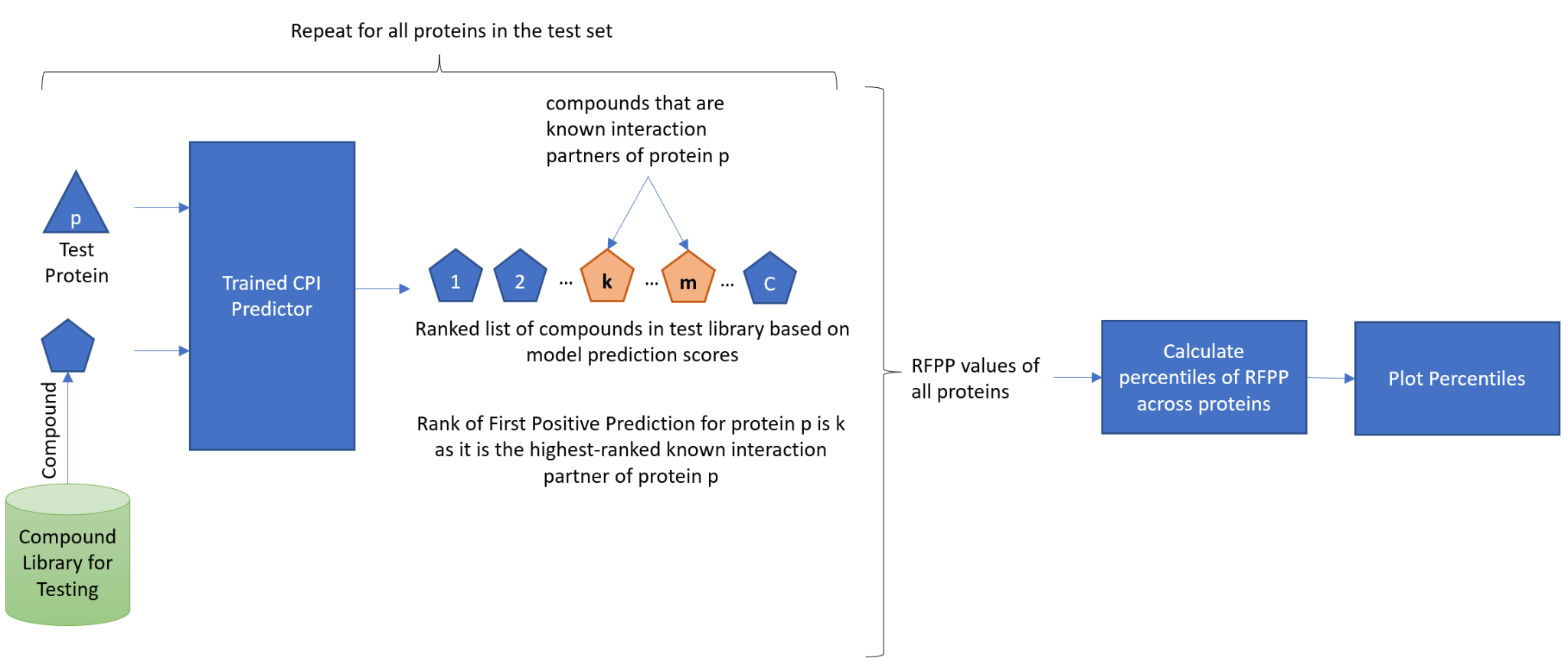


Figure 2 Steps in RFPP calculation

Table 1 Comparison of non-redundant cross-validation (CV) results of our proposed model with previous method CPI-NN using 40% reduendency removal of HCPI data by CPI-NN NR-HCPI is the non-redundant Human dataset having unique positive examples HCPI and randomly generated negative examples at different P: N ratios mentioned in the table.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Dataset | P: N | Total  (P+N) | CPI-NN | | Proposed | |
| AUC-ROC | AUC-PR | AUC-ROC | AUC-PR |
| NR-HCPI  (40%) | 1:1 | 5994 | 92.98 ± 0.87 | 91.62 ± 1.29 | 93.04 ± 0.35 | 93.86 ± 1.01 |
| NR-HCPI (NRCV) (40%) | 1:1 | 5266 | 61.59 ± 0.774 | 71.81± 0.395 | 69.02± 2.44 | 0.768 ± 0.0461 |

Table 2 cross-validation (CV) with (1:3)P:N ratio

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **cross-validation (CV) at different P: N ratios** | | | **Replacing testing negative with true Negative BindingDB Examples** | |
| **Alpha** | **AUC-ROC** | **AUC-PR** | **AUC-ROC** | **AUC-PR** |
| 1.0 | 0.7089 ± 0.0244 | 0.6267 ± 0.0174 | 0.9171 ± 0.0217 | 0.8806 ± 0.0184 |
| 0.9 | 0.7244 ± 0.0547 | 0.6519 ± 0.0458 | 0.9192 ± 0.0209 | 0.8681 ± 0.0179 |
| 0.8 | 0.7299 ± 0.0337 | 0.6565 ± 0.0249 | 0.9145 ± 0.0365 | 0.8149 ± 0.0457 |
| 0.7 | 0.7331 ± 0.0227 | 0.6572 ± 0.0138 | 0.9152 ± 0.0157 | 0.8086 ± 0.0274 |
| 0.6 | 0.7488 ± 0.0604 | 0.6767 ± 0.0427 | 0.9105 ± 0.0266 | 0.7624 ± 0.0185 |
| 0.5 | 0.7535 ± 0.047 | 0.6765 ± 0.0309 | 0.9089 ± 0.0198 | 0.7779 ± 0.038 |
| 0.4 | 0.7839 ± 0.0602 | 0.7146 ± 0.0468 | 0.9043 ± 0.0116 | 0.7245 ± 0.0171 |
| 0.3 | 0.7979 ± 0.047 | 0.7385 ± 0.028 | 0.8972 ± 0.0189 | 0.6582 ± 0.0208 |
| 0.2 | 0.8265 ± 0.0244 | 0.7729 ± 0.0218 | 0.8672 ± 0.0145 | 0.5571 ± 0.0126 |
| 0.1 | 0.8884 ± 0.0167 | 0.8416 ± 0.0171 | 0.8218 ± 0.0256 | 0.466 ± 0.0137 |
| 0.05 | 0.9474 ± 0.0125 | 0.9249 ± 0.0138 | 0.7673 ± 0.0144 | 0.3854 ± 0.0144 |
| 0.01 | 0.9831 ± 0.013 | 0.955 ± 0.0455 | 0.6735 ± 0.0053 | 0.3224 ± 0.0407 |

**Table 3** 5 cross-validation (CV) with (1:5)P:N ratio

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **cross-validation (CV) at different P: N ratios** | | | **Replacing testing negative with true Negative BindingDB Examples** | |
| **Alpha** | **AUC-ROC** | **AUC-PR** | **AUC-ROC** | **AUC-PR** |
| 1.0 | 0.7068 ± 0.0653 | 0.5711 ± 0.0541 | 0.9225 ± 0.0198 | 0.8942 ± 0.0194 |
| 0.9 | 0.7265 ± 0.0295 | 0.6012 ± 0.0344 | 0.9239 ± 0.026 | 0.8848 ± 0.0272 |
| 0.8 | 0.7286 ± 0.0405 | 0.5871 ± 0.0365 | 0.9249 ± 0.0242 | 0.8804 ± 0.0219 |
| 0.7 | 0.7377 ± 0.0467 | 0.6015 ± 0.0438 | 0.919 ± 0.0223 | 0.8492 ± 0.0251 |
| 0.6 | 0.7352 ± 0.0336 | 0.5904 ± 0.0341 | 0.9247 ± 0.0215 | 0.8582 ± 0.0155 |
| 0.5 | 0.7584 ± 0.0324 | 0.6262 ± 0.0223 | 0.9147 ± 0.0165 | 0.819 ± 0.0249 |
| 0.4 | 0.7714 ± 0.0522 | 0.6434 ± 0.0487 | 0.9196 ± 0.0381 | 0.8053 ± 0.0348 |
| 0.3 | 0.7951 ± 0.0267 | 0.678 ± 0.0235 | 0.9013 ± 0.0258 | 0.7127 ± 0.0346 |
| 0.2 | 0.8368 ± 0.0447 | 0.737 ± 0.0498 | 0.8714 ± 0.0157 | 0.5757 ± 0.0345 |
| 0.1 | 0.8963 ± 0.0257 | 0.818 ± 0.0305 | 0.8274 ± 0.0233 | 0.481 ± 0.0201 |
| 0.05 | 0.9484 ± 0.0148 | 0.8989 ± 0.0253 | 0.7742 ± 0.0183 | 0.3947 ± 0.0391 |
| 0.01 | 0.9731 ± 0.013 | 0.945 ± 0.0455 | 0.6966 ± 0.0118 | 0.3502 ± 0.0486 |

Table 4 ACE2’s top 100 Compounds predicted by our proposed model

|  |  |
| --- | --- |
| ACE2 Median Rank | ACE2Names |
| 1 | glycerol |
| 2 | dexfosfoserine |
| 3 | trandolapril |
| 4 | dimethyl sulfoxide |
| 6 | adenosine triphosphate |
| 6 | ramipril |
| 7 | N-Acetylglucosamine |
| 7 | perindopril |
| 8 | cysteine |
| 9 | cacodylic acid |
| 10 | glycine |
| 11 | sunitinib |
| 12 | mercaptamine |
| 15 | octanoic acid |
| 16 | 1-Octacosanol |
| 16 | diiodohydroxypropane |
| 17 | cetyl alcohol |
| 18 | docosanol |
| 18 | ferric hydroxide |
| 21 | xenon (127Xe) gas |
| 22 | Molybdenum Mo-99 |
| 23 | thallous chloride Tl-201 |
| 23 | glycolic acid |
| 23 | propylene glycol |
| 24 | dimercaprol |
| 25 | cystine |
| 27 | itramin tosilate |
| 29 | dasatinib |
| 30 | krypton (81mKr) gas |
| 30 | inositol |
| 31 | xenon |
| 32 | cholic acid |
| 34 | lactic acid |
| 34 | iodine |
| 35 | trichloroacetic acid |
| 35 | succimer |
| 36 | glutathione |
| 38 | glutamic acid |
| 38 | iodoform |
| 39 | xenon (133Xe) gas |
| 40 | mercuric amidochloride |
| 42 | glucose |
| 43 | galactose |
| 43 | iopydol |
| 44 | bromoform |
| 46 | vorinostat |
| 47 | dodecanoic acid |
| 47 | xylitol |
| 48 | docosanoic acid |
| 48 | sulfur hexafluoride |
| 48 | tetrachloroethylene |
| 49 | stearic acid |
| 49 | ethambutol |
| 52 | aminohydroxybutyric acid |
| 54 | cupric chloride |
| 55 | aluminium oxide |
| 57 | trichloroethylene |
| 58 | mercuric chloride |
| 62 | sorafenib |
| 62 | carbocloral |
| 62 | stannous fluoride |
| 63 | zinc oxide |
| 63 | imatinib |
| 64 | fomepizole |
| 65 | carbon tetrachloride |
| 67 | trometamol |
| 67 | migalastat |
| 68 | thiram |
| 69 | chromic chloride |
| 70 | glucose-1-phosphate |
| 73 | sucrose |
| 74 | algeldrate |
| 74 | fosfestrol |
| 74 | cupric oxide |
| 74 | ferrous chloride |
| 75 | methylpentynol |
| 76 | phenylalanine |
| 77 | lactose |
| 77 | perflunafene |
| 77 | mecysteine |
| 78 | maltose |
| 80 | symclosene |
| 81 | chloralodol |
| 83 | flurotyl |
| 83 | tribromoethanol |
| 84 | pyridoxal phosphate |
| 85 | unithiol |
| 86 | mercuric iodide |
| 87 | aspartic acid |
| 88 | mitolactol |
| 89 | phenol |
| 89 | mitobronitol |
| 90 | pentaerithrityl tetranitrate |
| 93 | pentaerythritol |
| 94 | streptozocin |
| 94 | fytic acid |
| 94 | propiolactone |
| 95 | isosorbide |
| 96 | moroxydine |

Table 5 Sars-Cov-2 Spike protein’s top 100 Compounds predicted by our proposed model

|  |  |
| --- | --- |
| Spike Median Rank | SpikeNames |
| 1 | glycerol |
| 2 | dexfosfoserine |
| 4 | N-Acetylglucosamine |
| 4 | dimethyl sulfoxide |
| 6 | sunitinib |
| 6 | adenosine triphosphate |
| 7 | glycine |
| 9 | cacodylic acid |
| 11 | cysteine |
| 11 | glutamic acid |
| 12 | dasatinib |
| 12 | nilotinib |
| 13 | mercaptamine |
| 13 | sorafenib |
| 14 | cetyl alcohol |
| 15 | docosanol |
| 16 | 1-Octacosanol |
| 20 | cystine |
| 21 | lovastatin |
| 23 | ferric hydroxide |
| 24 | Molybdenum Mo-99 |
| 24 | xenon (127Xe) gas |
| 25 | thallous chloride Tl-201 |
| 25 | glucose |
| 26 | itramin tosilate |
| 26 | galactose |
| 27 | glycolic acid |
| 28 | octanoic acid |
| 29 | trichloroacetic acid |
| 29 | diiodohydroxypropane |
| 30 | xenon |
| 35 | pyridoxal phosphate |
| 37 | aminohydroxybutyric acid |
| 37 | glutathione |
| 38 | iopydol |
| 38 | inositol |
| 40 | krypton (81mKr) gas |
| 41 | glucose-1-phosphate |
| 42 | mercuric amidochloride |
| 42 | streptozocin |
| 43 | dimercaprol |
| 43 | xenon (133Xe) gas |
| 44 | cholic acid |
| 44 | sucrose |
| 44 | voglibose |
| 47 | succimer |
| 48 | iodine |
| 49 | iodoform |
| 50 | lactic acid |
| 50 | lactose |
| 50 | propylene glycol |
| 51 | bromoform |
| 51 | maltose |
| 52 | imatinib |
| 53 | sulfur hexafluoride |
| 54 | stearic acid |
| 54 | aluminium oxide |
| 55 | docosanoic acid |
| 55 | fosfestrol |
| 56 | dodecanoic acid |
| 57 | phenol |
| 59 | propiolactone |
| 60 | aspartic acid |
| 62 | zinc oxide |
| 63 | aminolevulinic acid |
| 63 | mercuric chloride |
| 64 | erlotinib |
| 69 | xylitol |
| 69 | trometamol |
| 72 | fomepizole |
| 73 | migalastat |
| 74 | ethambutol |
| 75 | algeldrate |
| 77 | stannous fluoride |
| 79 | cupric chloride |
| 80 | flurotyl |
| 80 | fludeoxyglucose (18F) |
| 81 | carbon tetrachloride |
| 81 | perflunafene |
| 83 | carbocloral |
| 83 | symclosene |
| 85 | monoctanoin |
| 85 | tetrachloroethylene |
| 85 | thiram |
| 86 | norethisterone |
| 86 | phenelzine |
| 89 | trichloroethylene |
| 89 | mercuric iodide |
| 90 | fludarabine phosphate |
| 91 | chromic chloride |
| 91 | isosorbide |
| 93 | DL-Alanine |
| 94 | alanine |
| 94 | cupric oxide |
| 95 | mitolactol |
| 95 | chloralodol |
| 96 | pentaerythritol |
| 96 | mitobronitol |
| 96 | pentaerithrityl tetranitrate |