

**Table S1.** Contribution of the descriptors and its predicted activity - Model 2

| <b>Compound Name</b> | <b>Dataset split</b> | <b>ATSC4m</b> | <b>AATSC7i</b> | <b>GATS5c</b> | <b>SpMax5_Bhm</b> | <b>hmin</b> | <b>Exp. activity pIC50</b> | <b>Model predicted activity</b> |
|----------------------|----------------------|---------------|----------------|---------------|-------------------|-------------|----------------------------|---------------------------------|
| <b>A1</b>            | Excluded             | -150.613      | 0.16999        | 1.42508       | 3.125674028       | 0.025416    | -1.19866                   |                                 |
| <b>A2</b>            | Training             | -566.95       | 0.148565       | 1.322089      | 3.315003422       | 0.013312    | -0.71767                   | -0.7177                         |
| <b>A3</b>            | Training             | -363.531      | 0.300571       | 1.245976      | 3.139123587       | 0.037135    | -0.65418                   | -0.6542                         |
| <b>A4</b>            | Training             | -1158.25      | 0.10946        | 1.347909      | 3.448229765       | 0.012974    | -0.76042                   | -0.7604                         |
| <b>A5</b>            | Training             | -1849.53      | 0.063419       | 1.388731      | 3.451318505       | 0.01317     | -0.84011                   | -0.8401                         |
| <b>A6</b>            | Training             | -434.373      | 0.189907       | 1.338616      | 3.29591003        | 0.033856    | -0.93852                   | -0.9385                         |
| <b>A7</b>            | Training             | -144.952      | 0.077896       | 1.379928      | 3.142732176       | 0.013698    | -0.65128                   | -0.6513                         |
| <b>A8</b>            | Training             | -473.824      | 0.215142       | 1.086649      | 3.151668164       | 0.020063    | -0.38382                   | -0.3838                         |
| <b>A9</b>            | Training             | -170.971      | 0.426573       | 1.004151      | 3.417292915       | 0.039043    | -0.86213                   | -0.8621                         |
| <b>A10</b>           | Training             | -275.883      | 0.16498        | 1.091155      | 3.135368648       | 0.029323    | -0.42325                   | -0.4233                         |
| <b>A11</b>           | Prediction           | -351.663      | 0.109021       | 1.331711      | 3.200803294       | 0.018424    | -0.63749                   | -0.6375                         |
| <b>A12</b>           | Training             | 293.3892      | 0.222251       | 1.264795      | 3.341759912       | -0.01408    | -0.77597                   | -0.776                          |
| <b>A13</b>           | Training             | -327.75       | 0.083413       | 1.33318       | 3.210689641       | 0.024596    | -0.89209                   | -0.8921                         |
| <b>A14</b>           | Prediction           | -673.156      | 0.110354       | 1.287059      | 3.389979292       | 0.002123    | -0.7185                    | -0.7185                         |
| <b>A15</b>           | Training             | -422.907      | 0.212385       | 1.365634      | 3.151249129       | -0.00161    | -0.70927                   | -0.7093                         |
| <b>A16</b>           | Training             | -182.257      | 0.026798       | 1.323677      | 3.143652882       | 0.012183    | -0.40654                   | -0.4065                         |

|            |            |          |          |          |             |          |          |         |
|------------|------------|----------|----------|----------|-------------|----------|----------|---------|
| <b>A17</b> | Excluded   | -238.246 | 0.147417 | 1.409326 | 3.165794266 | 0.00683  | -0.42975 |         |
| <b>A18</b> | Training   | -294.377 | 0.188816 | 1.128388 | 3.445302924 | -0.03249 | -0.17609 | -0.1761 |
| <b>A19</b> | Training   | -416.36  | 0.052274 | 1.241908 | 3.133696389 | 0.045083 | -0.62737 | -0.6274 |
| <b>A20</b> | Excluded   | -212.48  | 0.185326 | 1.266641 | 3.352860035 | 0.023835 | -1.09621 |         |
| <b>A21</b> | Training   | -222.585 | 0.327564 | 1.194323 | 3.284275227 | 0.039924 | -1.05308 | -1.0531 |
| <b>A22</b> | Prediction | -102.236 | 0.082769 | 1.200738 | 3.453240814 | 0.033808 | -0.59879 | -0.5988 |
| <b>A23</b> | Training   | -804.624 | 0.091836 | 1.40347  | 3.303221314 | -0.00211 | -0.54283 | -0.5428 |
| <b>A24</b> | Training   | -436.695 | 0.106619 | 1.328013 | 3.147730981 | 0.0188   | -0.48855 | -0.4886 |
| <b>A25</b> | Training   | -331.053 | 0.229521 | 1.136152 | 3.303653226 | 0.004253 | -0.35218 | -0.3522 |
| <b>A26</b> | Training   | -511.048 | 0.166717 | 1.106404 | 3.313512999 | 0.037071 | -0.59218 | -0.5922 |
| <b>A27</b> | Training   | -497.33  | 0.179447 | 1.112946 | 3.302582849 | 0.013513 | -0.31175 | -0.3118 |
| <b>A28</b> | Prediction | -495.748 | 0.090511 | 1.20676  | 3.125788268 | 0.011527 | -0.45939 | -0.4594 |
| <b>A29</b> | Training   | -119.239 | 0.184796 | 1.449173 | 3.301426063 | 0.009606 | -1.16554 | -1.1655 |
| <b>A30</b> | Training   | -129.674 | 0.080919 | 1.422394 | 3.13276872  | 0.040722 | -1.0607  | -1.0607 |
| <b>A31</b> | Training   | -132.681 | 0.211961 | 1.454825 | 3.450396768 | 0.009165 | -1.22634 | -1.2263 |
| <b>A32</b> | Training   | -212.997 | 0.244178 | 1.456508 | 3.452942404 | 0.009421 | -1.26007 | -1.2601 |
| <b>A33</b> | Prediction | -208.635 | 0.179124 | 1.401204 | 3.179870948 | 0.016408 | -0.8704  | -0.8704 |
| <b>A34</b> | Training   | -158.595 | 0.061056 | 1.208048 | 3.493150991 | -0.17347 | 0.9914   | 0.9914  |

|     |          |          |          |         |            |          |          |        |
|-----|----------|----------|----------|---------|------------|----------|----------|--------|
| A35 | Training | -481.208 | 0.237308 | 1.17508 | 3.68518807 | -0.23563 | 1.236572 | 1.2366 |
|-----|----------|----------|----------|---------|------------|----------|----------|--------|