**Supplementary file 3**

Table summarizing the weights (wN) and performance (expressed as Pearson’s Coefficient R) of the 4-fold cross-validation, repeated 10 times, of the following binding affinity regression model:

ΔGcalc = w1 ICscharged/charged + w2 ICscharged\_apolar – w3 ICspolar/polar + w4 ICspolar/apolar

+ w5 %NISapolar + w6 %NIScharged + Q

Each coefficient has been reported as average on the four models trained on the respective folds.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | ***W1*** | ***W2*** | ***W3*** | ***W4*** | ***W5*** | ***W6*** | R  training | R  prediction |
| **4-fold1** | 0,09501 | 0,09982 | -0,19803 | 0,22253 | -0,19601 | -0,14249 | 0,75 | 0,68 |
| **4-fold2** | 0,09737 | 0,09845 | -0,18927 | 0,22174 | -0,18422 | -0,14123 | 0,74 | 0,68 |
| **4-fold3** | 0,09543 | 0,09781 | -0,20434 | 0,22816 | -0,18306 | -0,13461 | 0,74 | 0,70 |
| **4-fold4** | 0,09153 | 0,10596 | -0,18779 | 0,21853 | -0,18745 | -0,14614 | 0,75 | 0,66 |
| **4-fold5** | 0,09224 | 0,10091 | -0,19019 | 0,21989 | -0,18913 | -0,13950 | 0,74 | 0,65 |
| **4-fold6** | 0,09502 | 0,10067 | -0,19308 | 0,22218 | -0,19375 | -0,13557 | 0,75 | 0,68 |
| **4-fold7** | 0,09929 | 0,10402 | -0,17989 | 0,21283 | -0,18783 | -0,14139 | 0,75 | 0,65 |
| **4-fold8** | 0,07066 | 0,09868 | -0,19148 | 0,22295 | -0,18923 | -0,13625 | 0,74 | 0,71 |
| **4-fold9** | 0,09859 | 0,09860 | -0,18712 | 0,22188 | -0,18312 | -0,14454 | 0,74 | 0,70 |
| **4-fold10** | 0,09171 | 0,09868 | -0,19324 | 0,22670 | -0,18795 | -0,13899 | 0,75 | 0,65 |
|  |  |  |  |  |  |  |  |  |
| **Average** | 0,09268 | 0,10036 | -0,19144 | 0,22174 | -0,18817 | -0,14007 | 0,74 | 0,67 |
| **Standard**  **deviation** | 0,008 | 0,003 | 0,007 | 0,004 | 0,004 | 0,004 | 0,00 | 0,02 |