**Basak lab Descriptors:**

IC1 2.23 IC4 1.32

IC2 1.90 SIC3 1.27

ANZ4 1.58 AZN4 1.22

SIC 1 1.56 ANZ5 1.21

DN2N3 1.54 SIC2 1.20

**Diudea lab Descriptors:**

Variable Importance Variable Importance

PSA 2.51 PEOE1 1.83

Sum.of.topological.distances.between.O..O 2.35 E.state 1.66

E.state.topological.parameter 2.20 Superpendentic 1.49

ALOGP3 2.06 Topological.charge.index.of.order.5 1.31

Sum.of.topological.distances.between.N..O 1.99 PEOE12 1.28

**Combined Set of Descritors:**

Variable Importance Variable Importance

Sum.of.topological.distances.between.O..O 2.30 E.state 1.31

E.state.topological.parameter 2.22 Sum.of.topological.distances.between.N..O 1.21

PSA 1.56 Molecular.electrotopological.variation 1.12

Superpendentic 1.44 PEOE1 0.99

ALOGP3 1.37 PEOE12 0.87

**Basak Draft of mechanistic interpretation (2-14-2019)**

**Basak lab descriptors:**

Table 2 presents data on the subset of indices which are most influential in predicting BBB entry of chemicals. For the indices calculated using the POLLY [ ] and Triplet [ ] software by Basak laboratory, two classes of indices, viz. information theoretic neighborhood complexity indices and Triplet descriptors, emerged as the most influential in predicting BBB entry of chemicals. The IC1, IC2, SIC 1, SIC 3 and IC4 indices, developed by Basak et al [a ], are related to the overall heterogeneity of atomic neighborhoods in the molecular structure. Ooms et al. [b] reported that polarity of molecules is inversely correlated with the BBB permeability.

The ANZ4, AZN4, ANZ5, and DN2N3 are triplet descriptors developed by Balaban [c]. These are local vertex invariants (LOVI’s) which encode information for the presence of multiple bonds and/or heteroatoms in the molecular architecture. Consequently, these LOVis may represent polarity/ polarizability in the molecules. Li et al [d; Ref # 7 in our submitted paper] also found polarity of molecules to play in important role in the prediction of BBB partitioning of molecules. It is interesting to mention that topological descriptors were used in developing predictive QSAR models for a diverse set of 131 chemicals for different rat and human tissue: air partition coefficients, viz., blood: air, fat: air, brain: air, liver: air, muscle: air, and kidney: air [e].

**Diudea lab descriptors:** **Mircea and Claudiu to develop the first draft because most descriptors are from Diudea set.**

**Combined set of descriptors: Mircea and Claudiu to develop the first draft because most descriptors are from Diudea set.**

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