Constraints

1. Atom- and Bond-Based Indices

Two kinds of indices can be computed by **QUBILs-MAS** Software at present moment:

1. Atom-based indices
2. Bond-based descriptors

The main difference for these classes of descriptors is the relationship between elements in the molecular graph. In the first type, the relation is over pair of atoms and in the second type, the adjacency relation is at an edge level.

2. Chiral Indices (Coming soon)

The total and local quadratic, bilinear, and linear indices, as defined in their "standard" form in the **QuBiLS-MAS** module, cannot codify any information about the 3D molecular structure. In order to solve this problem, we introduced a *trigonometric 3D-chirality correction factor* in molecular vector $\bar{x}$. In this sense, a chirality molecular vector is obtained ($^{*}\bar{x}$), where the components of $\bar{x}$ (for instance, Pauling electronegativity (x_A) of the atom A) are substituted by the following term $[x_A + \sin((\omega_A+4\Delta)\pi/2)]$.

The *trigonometric 3D-chirality correction factor* uses a dummy variable ω_A, and an integer parameter Δ, where:

ω_A = 1 and Δ is an odd number when *A* has R (rectus), E (entgegen), or *a* (axial) notation according to Cahn-Ingold-Prelog rules

ω_A = 0 and Δ is an even number, if *A* does not have 3D specific enviroment

ω_A = -1 and Δ is an odd number when *A* has S (sinister), Z (zusammen), or *e* (equatorial) notation according to Cahn-Ingold-Prelog rules

Thus, this 3D-chirality factor $\sin((\omega_A+4\Delta)\pi/2)$ takes different values in order to codify specific stereo-chemical information such as chirality, Z/E isomerism, and so on. This factor therefore takes values in the following order 1 > 0 > -1 for atoms that have specific 3D environments. The chemical idea here is not that the attraction of electrons by an atom depends on their chirality, because experience shows that chirality does not change the electronegativities of atoms in the molecule over an isotropic environment in an observable way.

The present *trigonometric 3D-chiral correction factor* is invariant with respect to the selection of other chirality scales for all kinds of such chiral TIs (GBT-like ones). That is, the factor is always equal to 1, 0 or -1 for R, non-chiral or S atoms. As outlined above, invariance for this factor with respect to other 3D features such as *a*/*e* substitutions and Z/E or π-isomer is easily demonstrated by homology.

A very interesting point is that the present 3D-chiral (2.5) descriptor reduces to simple (2D) quadratic, bilinear and linear indices for molecules without specific 3D characteristics because $\sin(0+4\Delta)\pi/2 = 0$, being Δ zero or any even number. That is, when all the atoms in the molecule are not chiral, the **QuBiLS-MAS** MDs or any GBT-like chiral TI do not change upon the introduction of this factor.

3. N-tuples (Coming soon)

For **duplex (2),** the index calculations are performed over vertex pairs *i* and *j*. Here, the *nxn* k^{th} *non-stochastic graph–theoretic electronic-density matrix* of the molecular pseudo graph (*G*), $\mathbf{M}^{k}$, is used like matrix forms. For duplex relation, linear, quadratic and bilinear indices can be obtained. However, a generalization of these indices can be obtained using *n-linear maps* (*coming soon*).