

On quantum molecular similarity measures (QMSM) and indices (QMSI)*

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Quantum molecular similarity measures (QMSM) and the possibility to construct a discrete n -dimensional representation of any electronic structure is briefly described. The quantum molecular similarity indices (QMSI) are presented next. They constitute a possible transformation of the initial QMSM, intended to be useful in a great variety of applications. A set of diverse possibilities in QMSI definitions is given. A comparison of the indices obtained directly from electronic density distributions with those derived from the QMSM discrete representation of molecules leads to a handful of useful results, allowing a mathematical connection between the initial description of Carbó and the Hodgkin–Richards QMSI's. From the discussion of this kind of comparative reasoning a description of new index forms can be deduced. A brief numerical example is given.

1. Introduction

Quantum molecular similarity measures (QMSM) have been a subject of recent discussion and development [1]. Simultaneously with the definition of QMSM have evolved the quantum molecular similarity indices (QMSI) concepts, which in the seminal paper [1a] on the subject were defined as a correlation or cosine-like and as Euclidean distance-like indices. They constituted a pair of similarity and dissimilarity indices respectively. Following these early results, Hodgkin and Richards [2] have described a new index and claimed a better performance for this new form than the correlation-like one.

A thorough discussion on the meaning and usefulness of QMSM and QMSI has been carried out by Carbó and Domingo [1c], later on by Carbó and Calabuig [1i] and in recent reviews [1l–q]. Despite that, still the relationship between the various index options has been lacking in the literature. Thus, the purpose of this paper is to describe the possible relationship between various index definitions, as well as to use the newest QMSM theoretical developments in order to construct new

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QMSI, employing for this purpose the discrete n -dimensional representation of molecular electronic systems.

The first part of this work is concerned with a brief description of QMSM and QMSI. Also, the next task is to develop as much as possible the framework where molecules could be represented as n -dimensional points in Euclidean space. A comparison and study of the n -dimensional representation leads us to an interesting relationship between the aforementioned indices.

2. QMSM and QMSI

An unprecedented theoretical remark must be made before introducing the present subject of discussion. Once one has chosen the systems to study and an appropriate computational framework as well as a weighting operator, QMSM are uniquely defined. On the contrary, QMSI can be chosen within a great number of various mathematical manipulations, and can be considered as the result of some arbitrary transformation from the known QMSM as the starting point [11–n].

The basic knowledge attached to the QMSM framework has a very simple form. Suppose a set is known: $M = \{m_I\}$ composed of n molecules. Suppose also known is a set of density matrices [3], somehow associated in a one-to-one correspondence with the set $M : P = \{\rho_I\}$, that is,

$$\forall m_I \in M \rightarrow \exists \rho_I \in P \Rightarrow m_I \Leftrightarrow \rho_I; \quad \forall I. \quad (1)$$

Accepting this situation, then, from the quantum mechanical point of view, every molecule in M is represented by a density matrix in P . Thus, in this context a molecule is represented by a vector belonging to an ∞ -dimensional space. The definition of QMSM offers no difficulty whatsoever. Once a positive definite operator Ω is chosen, a QMSM between a pair of molecules $\{m_I, m_J\} \in M$ is obtained by choosing the pair of densities $\{\rho_I, \rho_J\} \in P$ and computing the integral

$$z_{JI}[\Omega] = \langle \rho_J | \Omega | \rho_I \rangle. \quad (2)$$

For the sake of simplicity, the presence of the operator following the symbol of the QMSM is taken away from the right side of eq. (2), unless one wants to stress the nature or the role of the definite positive operator Ω . Then, from the definition (2) one can construct an $(n \times n)$ *similarity matrix*: $Z = \{z_{JI}\}$. The similarity matrix can be partitioned in turn taking into account the fact one can consider the matrix Z as a row hypervector whose components are the matrix columns, defined easily as the elements of a vector set: $\{z_I = [z_{JI}], \forall J, I\} \in Z$. In this way, there can be established a new correspondence between the density set P and the column vector QMSM set Z :

$$\forall \rho_I \in P \rightarrow \exists z_I \in Z \Rightarrow \rho_I \Leftrightarrow z_I; \quad \forall I. \quad (3)$$

In this manner one can construct an n -dimensional representation of the mole-

cules belonging to the initial set M . The discrete n -dimensional description of a given molecule has been called a *point-molecule* [1g,11-n], and the name *molecular point-cloud* is used as a synonym of the set Z , collecting the point-molecules. QMSM constitute a natural vehicle leading towards the discrete n - dimensional description of molecular structures.

Once we have obtained the molecular point-cloud for the set M , QMSI can be obtained through mathematical manipulations performed over the elements of the similarity matrix Z . In the first paper discussing the nature of molecular similarity [1a], two classes of indices were described, as follows:

(a) *C-class*: A similarity index, commonly referred to as the Carbó index, which is nothing more than a member of the *correlation-like index* class. In fact, the mathematical interpretation of such an index is no more than the generalized form, most suitable in ∞ -dimensional functional spaces, of the cosine of the angle subtended by two density distributions, weighted by the positive definite operator Ω . The concrete form of this similarity index is written as

$$C_{JI} = Z_{JI}(Z_{JJ}Z_{II})^{-1/2}. \quad (4)$$

The similarity index has values in the interval $[0, 1]$. Both extreme values represent complete dissimilarity or total similarity respectively. These two extremal situations correspond to a couple of orthogonal or colinear density distributions. A fuzzy set framework [4] can be invoked at this moment, because the correlation-like similarity index may be interpreted as a fuzzy membership function defined over the Cartesian product: $P \otimes P$ [1c].

(b) *D-class*: A dissimilarity index, taking the form of an Euclidean distance belonging to a *distance-like index* class. The mathematical interpretation of this alternative manipulation of the QMSM matrix elements is such that it represents a distance, defined in ∞ -dimensional space, between two density distributions. The dissimilarity index may be defined as

$$D_{JI} = (z_{JJ} + z_{II} - 2z_{JI})^{1/2}. \quad (5)$$

The interval where the dissimilarity index values can be found is now: $[0, +\infty]$. The lower value corresponds this time to complete similarity, while the higher the index numerical value is found to be, then less similarity can be attached between both densities.

In the following discussion all the descriptions of possible QMSI will belong to one of the above described two classes: *C-class* or *D-class*, being complementary to each other. Inverse relationships between both index classes may be defined.

3. Generalized QMSI

There are many alternatives for generalized definitions of QMSI. Here some possible choices are given within the two described classes.

(1) D-class generalized indices:

(a) A generalized Euclidean distance-like index can have the following form:

$${}^{(g)}D_{JI}(K, X) = (K[z_{JJ} + z_{II}] - Xz_{JI})^{1/2}; \quad X \in [0, 2K], \quad (6)$$

which transforms into the Euclidean distance dissimilarity index as defined in eq. (5) when using $K = 1$ and $X = 2$.

(b) Another D-class index can be defined with the simple form

$${}^{(\infty)}D_{JI} = \max(z_{JJ}, z_{II}) \quad (7)$$

constituting a distance of infinite order.

(2) C-class generalized indices:

(a) The following form has the structure of a C-class family of indices. It has been proposed [1n] in order to generalize the Hodgkin–Richards [2] and Tanimoto [5] indices. The general function can be cast in the formula

$${}^{(g)}C_{JI}(K, X) = (2K - X)z_{JI}(D_{JI}(K, X))^{-2}; \quad K \in [0, 1], \quad (8)$$

where the generalized distance index described in equation (6) has been used too. When the parameters in the formula (8) take the values $K = 1$ and $X = 0$ the Hodgkin–Richards index is obtained, whereas the Tanimoto index appears naturally when $K = X = 1$.

(b) As a function of the D-class index of infinite order, the Petke index [6] can also be defined to have the form

$${}^{(\infty)}C_{JI} = z_{JI}({}^{(\infty)}D_{JI})^{-1}. \quad (9)$$

4. QMSI in the molecular point-cloud n -dimensional representation

The nature of the molecular point-cloud has not been used so far. Here the columns of the similarity matrix Z can be used directly to obtain new index forms. In fact, in this n -dimensional discrete representation of the molecules, one can even consider the possibility to construct point-molecules of larger dimensionality. Besides the sets used up to now, augmented sets may be gathered to obtain a great deal of information for the original molecular set M .

4.1. A NEW C-CLASS INDEX

One can augment the initial dimension of the molecular cloud Z by using the following procedure:

(a) Choose a new molecular set $A = \{a_I\}$ composed of m molecules and the associated density functions set $\sum = \{\sigma_I\}$, such that

$$\forall a_J \in A \rightarrow \exists \sigma_J \in \sum \Rightarrow a_J \Leftrightarrow \sigma_J. \quad (10)$$

(b) From here a set of column vectors $V = \{v_I\}$ can be obtained by computing the QMSM:

$$v_{JI} = \langle \sigma_J | \Omega | \rho_I \rangle; \quad \forall \sigma_J \in \sum \wedge \rho_I \in P. \quad (11)$$

(c) Then, a new augmented molecular point-cloud U may be constructed simply by the direct sum of the original molecular point-cloud Z and the new discrete vector set V , that is,

$$U = Z \oplus V = \{u_I = z_I \oplus v_I\}. \quad (12)$$

(d) Also, a new rectangular similarity matrix U of dimension $(d \times n)$ where $d = n + m$, whose columns are the augmented point-molecules $\{u_I\}$ can be constructed, and a Gramm matrix computed in the usual way:

$$S = U^T U. \quad (13)$$

(e) A new C-class index may be computed using the auxiliary quotient, which bears a D-class structure:

$${}^{(d)}\theta_{JI} = K(S_{JI})^{-1}, \quad (14)$$

where K is a scale factor. The definition (14) can be cast into the C-class index:

$${}^{(d)}C_{JI} = (1 + ({}^{(d)}\theta_{JI})^r)^{-1/r}, \quad (15)$$

where r is a positive integer.

4.2. ORIGIN OF THE NEW C-CLASS INDEX

The origin of such a C-class index as the one defined finally in eq. (15) may be easily seen when a (2×2) similarity submatrix is studied as a source of discrete molecular information. Such a matrix can be defined, once one has chosen two molecules $\{p, q\}$, as

$${}^{(2)}Z_{(p,q)} = ({}^{(2)}z_p, {}^{(2)}z_q), \quad (16)$$

where the two column vectors are written as

$${}^{(2)}z_p = \begin{pmatrix} z_{pp} \\ z_{pq} \end{pmatrix} \quad \wedge \quad {}^{(2)}z_q = \begin{pmatrix} z_{qp} \\ z_{qq} \end{pmatrix}. \quad (17)$$

where $z_{pq} = z_{qp}$. Then a C-class similarity index may be found for this two vectors as the correlation index:

$${}^{(2)}C_{pq} = ({}^{(2)}z_p \cdot {}^{(2)}z_q) (|{}^{(2)}z_p| |{}^{(2)}z_q|)^{-1} \quad (18)$$

and it is very easy, after a simple manipulation that it can be written as in eq. (15) above, by means of the D-class index:

$${}^{(2)}\theta_{pq} = \text{Det}|{}^{(2)}\mathbf{Z}_{(p,q)}|({}^{(2)}\mathbf{z}_p \cdot {}^{(2)}\mathbf{z}_q)^{-1}, \quad (19)$$

where $\text{Det}|{}^{(2)}\mathbf{Z}_{(p,q)}|$ is, in this case, the value taken by the scale factor K of definition (14).

4.3. RELATIONSHIPS BETWEEN C- AND D-CLASS QMSI

After the previous discussion on the many possible QMSI forms, one can present various connections between the indices, describing the relationships between the members of *C-* and *D-classes* and how they can be transformed from one class to another.

Knowing a set of D-class indices: $\{D_{JI}\}$, then it is easy to obtain a new set of C-class indices: $\{C_{JI}\}$, and vice versa, using any of the following recipes:

(1) D-class to C-class:

$$\begin{aligned} \text{(a)} \quad & {}^{(m)}C_{JI} = 1 - (D_{JI}[\text{Max}\{\forall\{J, I\}\}(D_{JI})]^{-1}). \\ \text{(b)} \quad & {}^{(t)}C_{JI} = 1 - \tanh(D_{JI}). \\ \text{(c)} \quad & {}^{(p)}C_{JI} = (1 + (D_{JI})^p)^{-1/p}; \quad p > 0. \end{aligned} \quad (20)$$

(2) C-class to D-class: Defining the factor K as a scale factor, one also has the transformations

$$\begin{aligned} \text{(a)} \quad & {}^{(a)}D_{JI} = K\pi^{-1} \arccos(C_{JI}). \\ \text{(b)} \quad & {}^{(l)}D_{JI} = K(1 - C_{JI}). \\ \text{(c)} \quad & {}^{(c)}D_{JI} = K(C_{JI})^{-1}(1 - C_{JI}). \end{aligned} \quad (21)$$

In this manner, a set of one class of indices can be transformed into the complementary class without problems. This allows a great freedom at the moment of using QMSI sets to obtain information, coming from the molecular point-cloud sets Z or U , which can be correlated with the characteristic properties of the electronic structure set M .

5. Some relationships related to C-class indices

In section 4.2 a very helpful but simple situation has been analyzed. This preparatory discussion may be used to find out the connection with the Hodgkin and Richards index and the initial C-class index defined by Carbó. The reasoning which follows proves that despite the apparent diversity between both indices, they are connected by the structure of the QMSM. Precisely, the presence in the theory of the duality between the ∞ -dimensional and n -dimensional representation of molecular electronic structures is the clue allowing to find out the connection between both indices.

Suppose the 2-dimensional case discussed above in section 4.2, the C-class index appearing in eq. (18) can also be interpreted as the cosine of the angle subtended by the 2-dimensional representations presented in eq. (17). Let us write the correspondence allowed for a C-class index, even if computed in a discrete 2-dimensional scenario, ${}^{(2)}C_{pq} = \cos(\gamma_{pq})$. Let us also take into account the cosine of the angle subtended by the two ∞ -dimensional density distributions, associated at the same time to the two molecular electronic structures and computed by the C-class Carbó index as

$$\cos^2(\alpha_{pq}) = (z_{pq})^2 (z_{pp}z_{qq})^{-1}. \quad (22)$$

The expression of the 2-dimensional D-class index ${}^{(2)}\theta_{pq}$ in eq. (19) may also be rewritten in another way, recalling:

$$\omega_{pq} = z_{pq}(z_{pp} + z_{qq})^{-1}, \quad (23)$$

which is nothing but half of the Hodgkin–Richards C- class index; then the ${}^{(2)}\theta_{pq}$ D-class index can be written as

$${}^{(2)}\theta_{pq} = \omega_{pq}(1 - \cos^{-2}(\alpha_{pq})), \quad (24)$$

so that $\cos(\gamma_{pq})$ may be written in the form as in eq. (18) in terms of ${}^{(2)}\theta_{pq}$, after a simple manipulation one has

$$\cos^{-2}(\gamma_{pq}) = 1 + \omega_{pq}^2 \operatorname{tg}^4(\alpha_{pq}). \quad (25)$$

Now calling $c_{pq} = \cos(\alpha_{pq})$, a final relationship between the indices is found to be

$$\omega_{pq} = \operatorname{tg}(\gamma_{pq}) c_{pq}^2 (1 - c_{pq}^2)^{-1}. \quad (26)$$

This means that there exists a direct relationship between the Hodgkin–Richards index, ω_{pq} , and the Carbó index, c_{pq} . The relationship involves the two subtended angles of the two molecular representations; in fact, eq. (26) above may also be written like a ratio between the tangents of the angles of both representations:

$$\omega_{pq} = \operatorname{tg}(\gamma_{pq}) \operatorname{tg}^{-2}(\alpha_{pq}). \quad (27)$$

Finally, an inverse relationship will give

$$c_{pq}^2 = \omega_{pq}(\operatorname{tg}(\gamma_{pq}) + \omega_{pq})^{-1}. \quad (28)$$

6. A short numerical example

Table 1 contains ordering information for five molecules: the methane and their four fluoro derivatives. Wavefunctions and geometries of these molecules have been obtained by means of the GAUSSIAN-90 program [8]. Full geometry optimization has been carried out using a 6-31G** [7] basis set. After the optimization,

Table 1
Ordering numbers of the methane and their four derivatives.

Number	Molecule
1	CH ₄
2	CH ₃ F
3	CH ₂ F ₂
4	CHF ₃
5	CF ₄

the MQSM between all the molecular pairs has been computed and listed in table 2. Also, for every molecular pair, the most representative QMSI are reported in table 2.

It can be seen from table 2 that the distance index of infinite order has a quite different behavior with respect to the other distance indices. The main difference is found in the diagonal elements of the matrix: there are no null elements. It can be seen how the Carbó and Hodgkin–Richards indices give similar values for every molecular pair. The Petke index attached to every molecular pair is a lower bound with respect to the corresponding Carbó index, as it can be easily deduced from their definitions. The Tanimoto index gives the lowest C-class index values while the $^{(2)}C_{pq}$ index returns the highest ones.

Table 2

Numerical values of the MQSM and QMSI for every molecular pair of table 1. SIM: QMSM $\Omega = I$; DST: distance index eq. (5); Dinf: distance index of infinite order eq. (7); $^{(2)}\theta_{pq}$: D-class index eq. (19); CAR: Carbó index eq. (4); HR: Hodgkin–Richards index eq. (8) with $K = 1$ and $X = 0$; TAN: Tanimoto index eq. (8) with $K = X = 1$; PET: Petke index eq. (9); $^{(2)}C_{pq}$: C-Class index eq. (15) ($r = 2$) obtained from $^{(2)}\theta_{pq}$.

Pair	SIM	DST	Dinf	$^{(2)}\theta_{pq}$	CAR	HR	TAN	PET	$^{(2)}C_{pq}$
1-1	0.318451	0.000000	0.318451	0.000000	1.000000	1.000000	1.000000	1.000000	1.000000
2-1	0.326555	0.362957	0.466397	0.163430	0.847339	0.832148	0.712546	0.700165	0.986907
2-2	0.466397	0.000000	0.466397	0.000000	1.000000	1.000000	1.000000	1.000000	1.000000
3-1	0.226270	0.515709	0.400045	0.468689	0.633945	0.629843	0.459687	0.565611	0.905480
3-2	0.321310	0.473098	0.466397	0.299356	0.743861	0.741677	0.589417	0.688920	0.957996
3-3	0.400045	0.000000	0.400045	0.000000	1.000000	1.000000	1.000000	1.000000	1.000000
4-1	0.173171	0.556129	0.337171	0.681591	0.528480	0.528265	0.358940	0.513600	0.826315
4-2	0.242239	0.564481	0.466397	0.506412	0.610859	0.602909	0.431545	0.519384	0.892127
4-3	0.292223	0.390858	0.400045	0.229722	0.795673	0.792774	0.656691	0.730475	0.974614
4-4	0.337171	0.000000	0.337171	0.000000	1.000000	1.000000	1.000000	1.000000	1.000000
5-1	0.140276	0.571390	0.318451	0.848162	0.462726	0.462165	0.300530	0.440495	0.762630
5-2	0.193919	0.605926	0.466397	0.662484	0.528572	0.513704	0.345627	0.415781	0.833656
5-3	0.228921	0.480406	0.400045	0.399911	0.673741	0.664857	0.497967	0.572238	0.928505
5-4	0.270797	0.290110	0.337171	0.141468	0.868121	0.865501	0.762892	0.803144	0.990141
5-5	0.288587	0.000000	0.288587	0.000000	1.000000	1.000000	1.000000	1.000000	1.000000

7. Conclusions

The dualistic point of view $\{\infty\text{-D}, n\text{-D}\}$ associated to the QMSM representation of molecular sets has interesting applications directed towards a large freedom to describe new QMSI. At the same time, this situation permits to find out conversion relationships between C-class and D-class indices, and hidden connections as the one obtained between Hodgkin–Richards and Carbó C-class index definitions.

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