Path Pendeccentric Connectivity Indices: Detour Matrix Based Molecular Descriptors for QSAR/QSPR Studies, Part 1: Development and Evaluation

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ABSTRACT

In the present study, highly sensitive detour matrix based molecular descriptors (MDs) termed as path pendeccentric connectivity indices 1-4 as well as their topochemical variants have been conceptualized. Proposed MDs are unique because they simultaneously take into consideration the cyclicity, path pendenticity, path eccentricity and augmented adjacency of each vertex in a hydrogen depleted molecular structure. An in-house computer program was also developed to calculate values of proposed MDs. Proposed MDs were evaluated for degeneracy, discriminating power, sensitivity towards relative position of substituent(s) in cyclic structures, branching and correlation with existing MDs. Highly encouraging results offer proposed MDs a vast potential for similarity/dissimilarity studies, characterization of structures, combinatorial library design, lead identification/optimization, pharmacokinetic relationship studies and QSAR/QSPR/QSTR studies. Proposed MDs will also take due care of shape factor, relative position (s) and presence of hetero atoms in chemical structures.

KEYWORDS
Detour Matrix, Hyper Detour Index, Path Pendeccentric Connectivity Indices 1-4, Superaugmented Pendentic Index

INTRODUCTION

The discovery of penicillin by Alexander Fleming is a scintillating example of serendipitous and fortuitous finding of drug. If luck favors, drug exploratory process may be accomplished through indiscriminate standardized experimentation or chemical perception where combinatorial libraries are synthesized and explored for biological activities. This methodology is highly time demanding, labor intensive and financially unviable. A rapid and financially viable approach to all these problems is to speculate prospective drug candidates before synthesis through utilization of computer aided drug development or design techniques like molecular modeling and simulation (Nantasenamat et al., 2009; Saliner, 2006).

The search for trends in the manner in which various properties of a molecule change depending upon their chemical structures is the main approach in (quantitative) structure-activity/property relationships [(Q)SAR/QSPR]. Finding of such a trend even for a narrow class of molecules is of great value. Such trends can be highly beneficial in the regularization of the behavior of molecules, especially in predicting the properties of other (sometimes hypothetical) molecules belonging to a particular/specific class. Moreover, the relationships/correlations between structures and properties
Molecular descriptors (MDs) play a vital role in establishing correlation between molecule and activity/toxicity/property because they can be easily used to express molecular topology in numerical form. Because of their relative complexity than simple atoms or groups or bonds count and less complexity than quantum-chemical parameters, MDs hold an important place in computational chemistry. Due to their simplicity, MDs can be calculated conveniently in a very short span of time with the help of simple software using input data on atom connectivity and can be utilized for quantitative structure activity/property/toxicity relationship [(Q)SAR/QSPR/QSTR] studies (Dong, & Guo, 2009; Balaban, & Ivanciuc, 1999).

It has been observed that it is a tedious job to discriminate every set of molecules even by the most discriminative descriptors. This indiscriminative behavior increases with increase in number of vertices/atoms in a graph. Consequently, MDs play a very crucial role. Accordingly, scientific community is continuously attempting to develop better MDs (Balaban & Ivanciuc, 1999; Vukicevic, & Balaban, 2005; Vukicevic, & Vojkovic, 2008).

Most of the topology based MDs are related to either topological distance in the graph or to vertex adjacency (atom-atom connectivity). Therefore, the distance matrix and adjacency matrix of molecular graphs constitute roots of said MDs (Sabljic, & Trinajstic, 1981). Only a small number of MDs based on pendent matrix have been reported in literature. These include superpendentic index (Gupta, Singh, & Madan, 1999), log of superpendentic index (Todeschini, & Consonni, 2000), terminal wiener index (Gutman, Furtula, & Petrovic, 2009), superaugmented pendent indices (Dureja, Kinkar, & Madan, 2009), super pendent topochemical index, pendent eccentricity index and pendent eccentricity topochemical index (Goyal, Dureja, Singh, & Madan, 2010). In an attempt to consider the peripheral and interior topology of a molecule simultaneously, detour matrix based MDs termed as path pendeccentric connectivity indices 1-4 (denoted by $^{PP\xi}_1$, $^{PP\xi}_2$, $^{PP\xi}_3$ and $^{PP\xi}_4$) as well as their topochemical variants termed as path pendeccentric connectivity topochemical indices (symbolized by $^{PPc\xi}_1$, $^{PPc\xi}_2$, $^{PPc\xi}_3$ and $^{PPc\xi}_4$) have been developed in the present study. As topostructural descriptors reveal information only about neighborhood and connectivity of atoms within the compound and ignore information related to chemical nature of atoms and bonds. Accordingly, topochemical variants of proposed MDs were developed so as to take into consideration the nature of atoms/bonds in a molecule (Bagchi, Maiti, Mills, & Basak, 2004). An in-house computer program was also developed to calculate values of proposed MDs for molecules containing at least one pendent atom/vertex. Newly proposed MDs were evaluated for degeneracy, discriminating power and sensitivity towards relative position of substituent(s) in cyclic structures, branching and correlation with existing MDs.

**METHODOLOGY**

**Calculation of Molecular Descriptors**

*Path Pendeccentric Connectivity Indices 1-4*

The path pendeccentric connectivity indices may be defined as the summation of the quotients, of the multiplication product of path pendenticity and augmented adjacency divided by path eccentricity...
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