Reviewer A:

My comments on the manuscript by Dr. Perdih are the same as I send before:

I think that people may be interested what are the best regression equation obtained by the author and how they compare with any published results obtained by regressions using the same number of descriptors, which appear to be four descriptors in this case. Perdih contnues to report various not optimal combinations of his descriptors- this at best belongs in my view to supplementry material, not in the main manuscript.

The paper is devoted to the illustration of the way of how to develop very good descriptors for the physicochemical properties of octane isomers using the mutually optimized combinations of vertex-degree weighted path indices combined with the vertex-degree vertex-distance weighted elements of the Universal matrix. It is devoted to the illustrating the procedure and not to mere comparison with existing results. It is the procedure, which is applicable to other physicochemical properties of octane isomers, and not the best descriptor for the boiling point of octanes. This is the reason, why the not optimal combinations are reported, since they illustrate the procedure of improving the results, which would be useful in other cases as well. On the other hand, they are needed to compare to the results of other descriptors, which the Reviewer A is demanding.

My second comments is (and this is not widely known among chemists using MRA (Multivariate Regression Analysis, MRA) that the coeficients of MRA do not give the interpretation of the role of individual descriptors, which one can obtain using stepwise regression, as is oulined in:

Resolution of Ambiguities in Structrure-Property Studies by Use of Orthogonal Descriptors, Chem. Inf. Comput. Sci. 367 (1991) 311-320.

I did not use the coefficients of MRA for the interpretation.

The reasons were illustrated in some previous papers, namely that it is not to consider only the coefficients of MRA (in my case k_N resp. k_{ij}) but the products $k_N \times \mathbf{PN}$ resp. $k_{ij} \times \mathbf{u}_{ij}$ and that they reflect in different proportions both the contribution to the "numerical volume" of the descriptor and to the goodness of correlation.

For illustration, in Table 4 the value of 3. represents the most of the "numerical volume" of the descriptor, whereas the decimals reflect that part of the descriptor that contributs to its goodness.

The author is reporting on the role of individual vertices in some octane isomers (see lines 146-160). How are this results obtained? He should illustrated this on one of the selected molecules mentioned.

As suggested by the referee the structure of a selected molecule was added into the manuscript for the sake of illustration and based on this structure the role of individual vertices in octanes was explained (Lines 219-262).

It is good to see Table 4 with illustration of the TI values.

I would like to see more comparsions with reproted results on the BP (boiing points) using other descriptors. For example, use of path/walk descriptors (See: On solved and Unsolved problems of Structural Chemistry (by M. RandIc, M. Novic and D. Plavsic) on p.161 (Table 6.7) reported for BP of octanes r = 0.9141 and s= 2.64. All the dozen best two descriptors regressions of Perdih listed of Table 2 are visibly better, which speak in favor oy his approach, though there may be additional regressions, particularly those using variable connectivity index, which may be comparable to those of Table 2. I would be intersted, for example, to see what would optimal path/walk descriptors give?

Path/walk descriptors: Performed according to reviewers suggestions (Lines 195-211).

Variable connectivity index: I did not notice any publication dealing with the boiling points of octane isomers but mainly with structures containing heteroatoms. So this question remains open. Anyway, it deserves a separate study.

RECOMMENDATION:

Paper could be published as it may stimulate others to search for optimal results using the variable molecular descriptors, which too few chemists have hitherto used. I also think that it would be desireable for commparison to see MRA based on conventional 2-4 descriptors, like results that can be obtained with CODESSA (A. R Katritsky, V. Lobanov and M. Karelson, Univ. of Florida, Gainesvelle, FL (1995).

Since the goodness of newly derived descriptors is, using the standard error S as a measure, between one and two orders of magnitude better than the published data obtained with the combination of two to three descriptors, I doubt that such comparisons with combinations of existing descriptors would result in better correlations. Furthermore, such comparison is out of the scope of current contribution. Interested authors are, however, free to perform that and challenge my approach.

Reviewer B:

The author successfully addressed all issues raised by this reviewer. Consequently, the manuscript has been significantly improved and can be in its current form recommended for publication in ACSi.