ACADEMIA ROMÂNĂ
Revue Roumaine de Chimie
https://www.icf.ro/rrch/

Rev. Roum. Chim.,
2026, *71*(5–6), 343–351
DOI: 10.33224/rrch.2026.71.5-6.05

Dedicated to Professor Alexandru T. Balaban on the occasion of his 95th anniversary

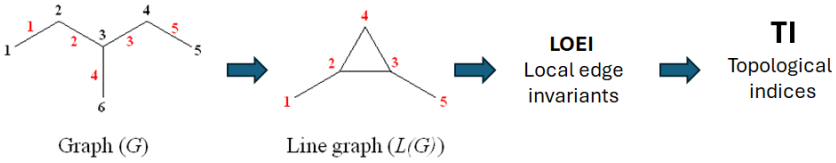
QSPR STUDIES USING NEW THIRD GENERATION TOPOLOGICAL INDICES. I. LOCAL EDGE INVARIANTS AND TOPOLOGICAL INDICES GENERATED FROM THE EDGE-ADJACENCY MATRIX OF MOLECULAR GRAPHS

Paul I. SEZONOV,[a,*] Andrei T. PANTEA,[b] Adrian BETERINGHE[c] and Petru I. FILIP[a]

[a] "Costin D. Nenitescu" Institute of Organic and Supramolecular Chemistry, Roumanian Academy, 202B Splaiul Independenței, 060023 Bucharest, Roumania
[b] Department of Applied Mathematics, Centre for Applied Mathematics, CNRS, École Polytechnique, Institut Polytechnique de Paris, 91120, Palaiseau, France
[c] Danubius University of Galati, 800654 Galati, Roumania

Received January 21, 2026

Third-generation topological indices (TIs) have been developed based on the edge-adjacency matrix of a molecular graph. Initially, real-valued Local Edge Invariants (LOEIs) are obtained by solving a system of linear equations constructed from this matrix.



In this system, bond-related properties – such as bond energy, bond length, and the sum of Van der Waals radii – are incorporated as diagonal elements, while the free terms consist of local edge descriptors, including the number of hydrogen atoms attached to a given bond and the edge degree (defined as the sum of the degrees of the connected vertices). These LOEIs are then combined using simple mathematical expressions to generate the corresponding topological indices. The resulting TIs are subsequently employed in quantitative structure–property relationship (QSPR) studies to model various properties of C5–C9 alkanes.

INTRODUCTION

Eight decades ago, topological indices based on molecular graph theory were first utilized in the development of quantitative structure-property relationships (QSPR). The field quickly expanded to include structure-activity relationships (QSAR), similarity/diversity analysis of molecular libraries, and various other related areas.[1,2] QSAR started with the work of Corwin Hansch relating chemical structure with biological activity and partition coefficients of phenoxy acetic acids,[3] but structure-activity relations have been postulated much earlier.[4] Today a few thousands of different molecular descriptors and Tis[3,5,6] are used in such studies and there are quite a few dedicated software packages.[7–11]

Professor Balaban identified in 1992, successive generations of topological indices:[12] first-generation TI's which were integer numbers obtained by

* Corresponding author: paul.sezonov@gmail.com

simple arithmetic from local vertex invariants (LOVI's), which were integer numbers; second-generation TI's which were real numbers obtained via sophisticated operations from integer LOVI's and third-generation TI's which are real numbers based on real-number LOVI's.

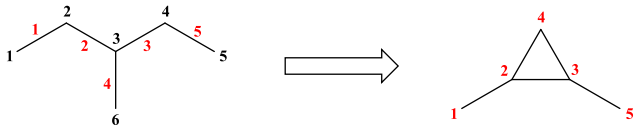
Some of the third generation TI's were obtained as solutions of a system of linear equations generated from triplets consisting of a matrix (adjacency or distance matrix) and two column vectors containing properties specific to the atoms represented by the vertices of the molecular graph (*e.g.,* Z, atomic mass, Van der Waals radius, first ionization potential, etc.) or local vertex invariants (vertex degree, sum of distances for that vertex, etc.).[13] The elements of the two vectors can be used as diagonal terms in the systems matrix having the adjacency or distance matrix as off diagonal terms, or as the vector of free terms of the linear system.

We are reporting here a method to obtain third-generation TI's starting from the edge-adjacency matrix of a molecular graph and also structure-properties correlations based on them for alkanes having up to 10 carbon atoms.

MATERIALS AND METHODS

The edge-adjacency matrix[14] of a simple graph, denoted ^{e}A, is a square matrix of dimension equal to the number of edges of the graph, having $a_{ij} = 1$ if edges labeled *i* and *j* are incident having a common endpoint, and $a_{ij} = 0$ otherwise.

Also, ^{e}A can be defined based on the line-graph[15] L(*G*) of a simple graph G. In the line graph L(*G*) of a graph G each edge in *G*, becomes a vertex in L(*G*) and every two incident edges in *G* are generating an edge between their corresponding vertices in L(*G*). The adjacency matrix of L(*G*) is the edge-adjacency matrix of G. In Fig. 1 an example is given for the molecular graph and line-graph for 3-methyl-pentane and the corresponding adjacency and edge-adjacency matrices.



Graph (*G*) Line graph (*L(G)*)

$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \end{bmatrix} \qquad \begin{bmatrix} 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 1 & 1 & 0 \\ 0 & 1 & 0 & 1 & 1 \\ 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \end{bmatrix}$$

Adjacency matrix of *G* Adjacency matrix of *L(G)*
Edge-adjacency matrix of G

Fig. 1 – Molecular graph (G) and line graph L(G) for 3-methyl-pentane.

Building TIs based on local edge invariants (LOEI) was first presented by E. Estrada.[16] Later on many topological indices have been reformulated in terms of the edge-degrees instead of the vertex-degrees, *e.g.*, the reformulated Zagreb indices,[17,18] the edge-connectivity index,[17,19] the reformulated Gordon-Scantlebury index,[3] the reformulated Platt index.[3]

RESULTS AND DISCUSSION

We present here new TIs obtained by first generating real number LOEI's as solutions of a system of linear equations build starting from the edge adjacency matrix of the molecular graph, including bond properties (bond energy, bond length, sum of Van der Waals radii, etc.) as diagonal terms and having as free terms local edge invariants such as number of hydrogens attached to that edge/bond or the edge-degree defined as the sum of the degrees of the bonded vertices, then combining these LOEI's with simple formulas to generate TIs. The formulas tested to generate the TIs in this study are presented in Table 1.

In Fig. 2 an example of LOEI generation is illustrated for 3-methyl-pentane by solving the system of linear equations built from the edge-adjacency matrix using carbon-carbon single bond energy (kJ/mol divided by 100) as diagonal terms and edge-degrees as free terms. TIs calculated based on these LOEI's are presented in the same figure

Table 1

Formulas used to generate TI's based on LOEI's

$TI_1 = \sum_{i=1}^{nleg} LOEI_i$	$TI_2 = \sum_{i=1}^{nleg} \frac{1}{LOEI_i}$	$TI_3 = \sum_{i=1}^{nleg} \frac{1}{\sqrt{LOEI_i}}$
$TI_4 = \frac{1}{nbond} * \sqrt{\sum_{i=1}^{nbond} \frac{1}{LOEI_i^2}}$	$TI_5 = \sum_{i,j}^{adjacent} \frac{1}{\sqrt{LOEI_i * LOEI_j}}$ Sum over all pairs of adjacent edges	$TI_6 = \frac{1}{npairs} \sum_{i,j}^{adjacent} \frac{1}{\sqrt{LOEI_i * LOEI_j}}$

$$\begin{bmatrix} 3.46 & 1.00 & 0.00 & 0.00 & 0.00 \\ 1.00 & 3.46 & 1.00 & 1.00 & 0.00 \\ 0.00 & 1.00 & 3.46 & 1.00 & 1.00 \\ 0.00 & 1.00 & 1.00 & 3.46 & 0.00 \\ 0.00 & 0.00 & 1.00 & 0.00 & 3.46 \end{bmatrix} * \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \end{bmatrix} = \begin{bmatrix} 3.00 \\ 5.00 \\ 5.00 \\ 4.00 \\ 3.00 \end{bmatrix} \Rightarrow \begin{matrix} x_1 = 0.6275914056 \\ x_2 = 0.8285337366 \\ x_3 = 0.8285337366 \\ x_4 = 0.6771481291 \\ x_5 = 0.6275914056 \end{matrix}$$

TI_1=3.58940 TI_2=7.07747 TI_3=5.93705 TI_4=0.63788 TI_5=6.65064 TI_6=1.33013

Fig. 2 – LOEI's and TI's generated for the line graph L(G) for 3-methyl-pentane by solving the system of linear equations built from the edge-adjacency matrix using carbon-carbon single bond energy (kJ/mol divided by 100) as diagonal terms and edge-degrees as free terms.

Further on we tested the LOEI based TIs in QSAR correlations with experimental molecular properties of C5–C9 alkanes presented in scientific publications: molar volume,[16] molar refraction[16] and some thermodynamic properties.[20] Values of the computed topological indices are presented in Table 2. In the table are also included, in last column, values for a topological index (TI $_{lovi}$) generated based on local vertex invariants (LOVI) of the molecular graph according to the method developed by us and presented in a previous paper.[13] This TI has been used in bilinear regression analyses that are part of this work.

Table 2

Topological indices TI_1–TI_6 and TI $_{lovi}$ computed for C5–C9 alkanes

Compound	TI_1	TI_2	TI_3	TI_4	TI_5	TI_6	TI $_{lovi}$
n Pentane	2.80218	5.73976	4.78843	0.71934	4.19372	1.39791	1.03030
2-methyl-butane	2.88636	5.62013	4.73343	0.70709	5.36271	1.34068	0.98614
2,2-dimethyl-propane	3.09598	5.16800	4.54665	0.64600	7.75200	1.29200	0.87500
n Hexane	3.53359	7.11376	5.95986	0.63803	5.55643	1.38911	1.28033
2-methyl-pentane	3.63256	6.91875	5.87783	0.62040	6.75373	1.35075	1.23461
3-methyl-pentane	3.58940	7.07747	5.93705	0.63788	6.65064	1.33013	1.24371
2,2-dimethyl-butane	3.76131	6.75932	5.80117	0.60975	8.98723	1.28389	1.14209
2,3-dimethyl-butane	3.68452	6.89487	5.86083	0.62074	7.89477	1.31580	1.20000
n Heptane	4.26657	8.47541	7.12705	0.57800	6.92200	1.38440	1.53033
2-methyl-hexane	4.36078	8.31099	7.05577	0.56732	8.11249	1.35208	1.48487
3-methyl-hexane	4.33139	8.40088	7.09026	0.57461	8.03545	1.33924	1.49241
3-ethyl-pentane	4.30593	8.47007	7.11728	0.58003	7.96105	1.32684	1.50000
2,2-dimethyl-pentane	4.51427	8.03026	6.93537	0.54823	10.38706	1.29838	1.38914
2,3-dimethyl-pentane	4.39677	8.31752	7.05114	0.56997	9.18681	1.31240	1.45621
2,4-dimethyl-pentane	4.46914	8.07603	6.95885	0.55019	9.31953	1.33136	1.43750
3,3-dimethyl-pentane	4.43988	8.29192	7.03394	0.57036	10.23172	1.27897	1.40787
2,2,3-trimethyl-butane	4.54309	8.06706	6.94314	0.55290	11.52601	1.28067	1.36464

n Octane	4.99905	9.84163	8.29580	0.53252	8.28687	1.38115	1.78033
2-methyl-heptane	5.09477	9.66554	8.22047	0.52315	9.47892	1.35413	1.73483
3-methyl-heptane	5.06100	9.78309	8.26468	0.53094	9.39540	1.34220	1.74263
4-methyl-heptane	5.07463	9.71538	8.24036	0.52618	9.42207	1.34601	1.74107
3-ethyl-hexane	5.04388	9.81807	8.27914	0.53295	9.33952	1.33422	1.74892
2,2-dimethyl-hexane	5.24027	9.43467	8.11766	0.51167	11.74436	1.30493	1.63965
2,3-dimethyl-hexane	5.13601	9.65471	8.20940	0.52404	10.57058	1.32132	1.70515
2,4-dimethyl-hexane	5.16525	9.57195	8.17633	0.51919	10.60001	1.32500	1.69553
2,5-dimethyl-hexane	5.18590	9.51852	8.15544	0.51572	10.66819	1.33352	1.68966
3,3-dimethyl-hexane	5.18919	9.58354	8.17552	0.52122	11.62770	1.29197	1.65515
3,4-dimethyl-hexane	5.10538	9.75913	8.24838	0.53113	10.47636	1.30954	1.71265
2-methyl-3-ethyl-pentane	5.12189	9.67664	8.21873	0.52534	10.50350	1.31294	1.71113
3-methyl-3-ethyl-pentane	5.13094	9.76872	8.24614	0.53326	11.48680	1.27631	1.67234
2,2,3-trimethyl-pentane	5.35512	9.17408	8.01109	0.49597	12.95513	1.29551	1.59052
2,2,4-trimethyl-pentane	5.35512	9.17408	8.01109	0.49597	12.95513	1.29551	1.59052
2,3,3-trimethyl-pentane	5.23017	9.57010	8.16430	0.52161	12.76807	1.27681	1.62903
2,3,4-trimethyl-pentane	5.20999	9.54091	8.15832	0.51851	11.72034	1.30226	1.66726
n Nonane	5.73169	11.20619	9.46398	0.49618	9.65190	1.37884	2.03033
2-methyl-octane	5.82693	11.03445	9.39015	0.48876	10.84365	1.35546	1.98484
3-methyl-octane	5.79455	11.14136	9.43067	0.49451	10.76161	1.34520	1.99260
4-methyl-octane	5.80383	11.10105	9.41598	0.49223	10.78166	1.34771	1.99130
3-ethyl-heptane	5.77480	11.19053	9.45018	0.49698	10.70080	1.33760	1.99911
4-ethyl-heptane	5.78307	11.15692	9.43783	0.49511	10.71967	1.33996	1.99780
2,2-dimethyl-heptane	5.97496	10.78446	9.28070	0.47818	13.11099	1.31110	1.88956
2,3-dimethyl-heptane	5.86651	11.03123	9.38179	0.48995	11.93036	1.32560	1.95533
2,4-dimethyl-heptane	5.90929	10.88140	9.32463	0.48203	11.98698	1.33189	1.94415
2,5-dimethyl-heptane	5.88701	10.98486	9.36231	0.48794	11.95097	1.32789	1.94738
2,6-dimethyl-heptane	5.92361	10.85164	9.31245	0.48055	12.03575	1.33731	1.93929
3,3-dimethyl-heptane	5.91641	10.97934	9.35478	0.48875	12.98536	1.29854	1.90562
3,4-dimethyl-heptane	5.84573	11.08918	9.40410	0.49305	11.86069	1.31785	1.96155
3,5-dimethyl-heptane	5.86257	11.05985	9.39095	0.49198	11.88034	1.32004	1.95353
4,4-dimethyl-heptane	5.93953	10.86806	9.31462	0.48228	13.02502	1.30250	1.90239
2-methyl-3-ethyl-hexane	5.85719	11.03843	9.38559	0.49018	11.88067	1.32007	1.96029
2-methyl-4-ethyl-hexane	5.85719	11.03843	9.38559	0.49018	11.88067	1.32007	1.96029
3-methyl-3-ethyl-hexane	5.87670	11.08064	9.39494	0.49386	12.87905	1.28791	1.91985
3-methyl-4-ethyl-hexane	5.82700	11.13712	9.42279	0.49557	11.79030	1.31003	1.96780
2,2,3-trimethyl-hexane	5.99901	10.81417	9.28658	0.48075	14.20170	1.29106	1.86859
2,2,4-trimethyl-hexane	6.04933	10.67907	9.23193	0.47426	14.23582	1.29417	1.84881
2,2,5-trimethyl-hexane	6.06395	10.64906	9.21986	0.47265	14.30068	1.30006	1.84469
2,3,3-trimethyl-hexane	5.97707	10.87305	9.31009	0.48366	14.16416	1.28765	1.87655
2,3,4-trimethyl-hexane	5.91623	10.99277	9.35948	0.48948	13.01076	1.30108	1.92394
2,3,5-trimethyl-hexane	5.96810	10.83327	9.29835	0.48092	13.13631	1.31363	1.90852
2,4,4-trimethyl-hexane	6.02766	10.73868	9.25543	0.47736	14.19569	1.29052	1.85677
3,3,4-trimethyl-hexane	5.94558	10.98665	9.35191	0.49020	14.05856	1.27805	1.88402
3,3-diethyl-pentane	5.83375	11.19206	9.43882	0.49949	12.75378	1.27538	1.93548

2,2-dimethyl-3-ethyl-pentane	5.99277	10.80587	9.28445	0.48020	14.13522	1.28502	1.87287
2,3-dimethyl-3-ethyl-pentane	5.92923	11.01857	9.36549	0.49159	14.02211	1.27474	1.89210
2,4-dimethyl-3-ethyl-pentane	5.94332	10.86690	9.31358	0.48232	13.04513	1.30451	1.92081
2,2,3,3-tetramethyl-pentane	6.08254	10.74412	9.24872	0.47908	16.41163	1.26243	1.80137
2,2,3,4-tetramethyl-pentane	6.07898	10.68122	9.22781	0.47522	15.34698	1.27892	1.82891
2,2,4,4-tetramethyl-pentane	6.24403	10.26394	9.06001	0.45391	16.59122	1.27625	1.74194
2,3,3,4-tetramethyl-pentane	6.02590	10.83445	9.28871	0.48282	15.29776	1.27481	1.84871

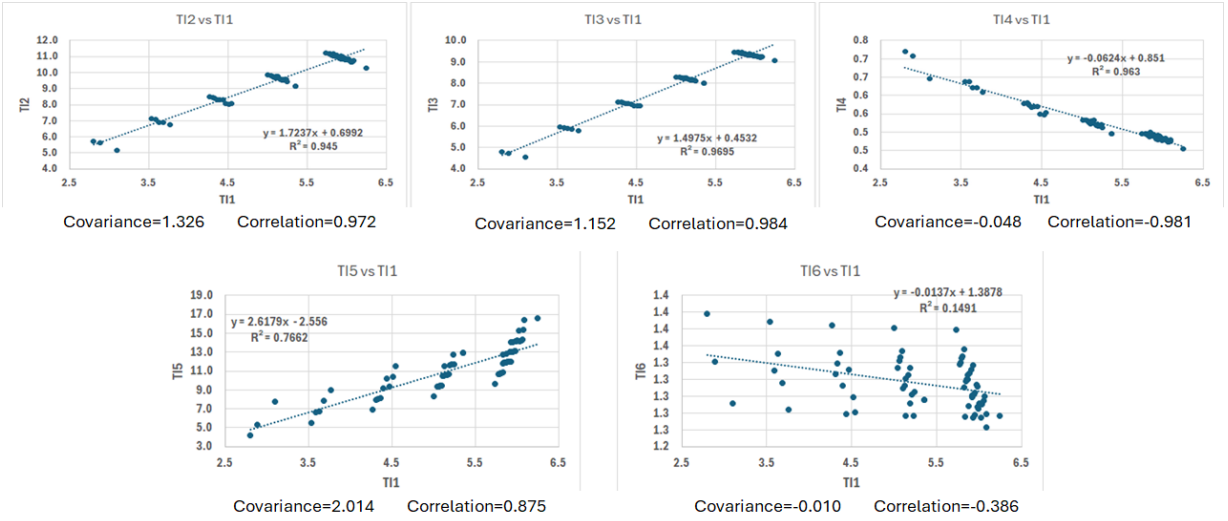


Fig. 3 – Linear relationships between TI_1 and TI_2–TI_6.

Local edge invariants, local vertex invariants and topological indices were generated using our own program and all data processing was done using EXCEL.

To assess the suitability of these TIs for use in multilinear QSAR/QSPR models, we evaluated their independence by calculating the covariance and correlation for each pair of indices. Figure 3 shows how TI_2–TI_6 are related to TI_1.

Similar graphs and calculations have been done for the rest of possible pairs of TIs, covariance and correlation being presented for each pair in Table 3. Values for correlation written in red in Table 3 indicate pairs of TIs which are close to linearly dependent and therefore not suitable to use together in multilinear regression studies.

Table 3

Covariance and Correlation value for all pairs of TIs computed for C5–C9 alkanes

		TI_1	**TI_2**	**TI_3**	**TI_4**	**TI_5**	**TI_6**
TI_1	Cov	1.000	1.326	1.152	–0.048	2.014	–0.011
	Corr	1.000	0.972	0.985	–0.981	0.875	–0.386
TI_2	Cov		1.000	2.071	–0.081	3.075	–0.011
	Corr		1.000	0.998	–0.937	0.754	–0.238
TI_3	Cov			1.000	–0.071	2.753	–0.011
	Corr			1.000	–0.954	0.787	–0.270
TI_4	Cov				1.000	–0.128	0.001
	Corr				1.000	–0.873	0.403
TI_5	Cov					1.000	–0.060
	Corr					1.000	–0.736
TI_6	Cov						1.000
	Corr						1.000

QSPR relationships have been generated as linear equations relating topological indices TI_1–TI_6 to molecular properties: molar volume, molar refraction, boiling point (BP, ºK), entropy (cal/K mol), heat capacity (Cp, cal/K mol), enthalpy of formation (ΔHf, Kcal/mol). In Fig. 4 are presented, as an example, the graphs and linear equations obtained for TI_1.

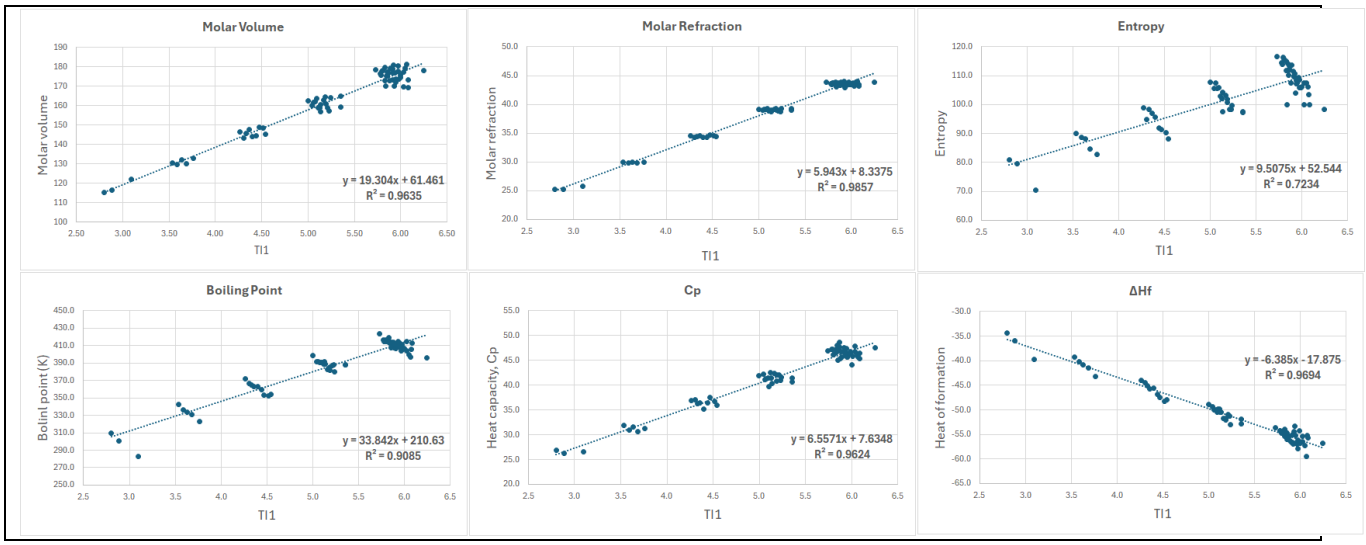


Fig. 4 – Linear relationships between TI1 and molecular properties of C5–C9 alkanes.

In Table 4 linear relationships between molecular properties and LOEI based TIs are shown. Best correlations for a molecular property are marked with green and the poor ones with two grades of pink. While TI_1–TI_3 have reasonably good correlations with most of the studied properties TI_4, TI_5 and TI_6 are less performant. The best linear equation is obtained for molar refraction correlated with TI_3 having R^2=0.9937 while the best equation for entropy has a correlation coefficient of R^2=0.8646. Overall the direct correlations of entropy with the individual TIs developed in this work give lower R^2 values than those obtained for other properties.

Table 4

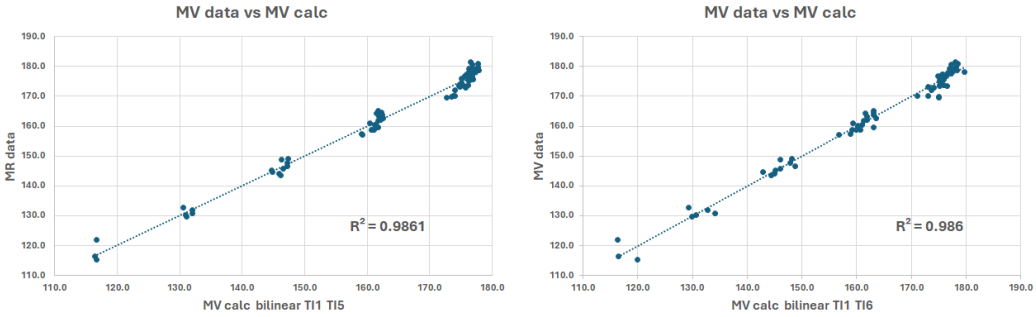
Linear relationships between TIs and molecular properties

	MV	MR	Entropy	BP	Cp	ΔHf
TI1	y = 19.304x + 61.461 R^2 = 0.9635	y = 5.943x + 8.337 R^2 = 0.9857	y = 9.507x + 52.544 R^2 = 0.7234	y = 33.842x + 210.63 R^2 = 0.9085	y = 6.557x + 7.634 R^2 = 0.9624	y = -6.385x - 17.875 R^2 = 0.9694
TI2	y = 10.797x + 57.543 R^2 = 0.9477	y = 3.343x + 6.944 R^2 = 0.9807	y = 5.862x + 45.317 R^2 = 0.8646	y = 19.824x + 195.04 R^2 = 0.9801	y = 3.713x + 5.855 R^2 = 0.9706	y = -3.444x - 17.813 R^2 = 0.887
TI3	y = 12.705x + 57.158 R^2 = 0.9655	y = 3.923x + 6.914 R^2 = 0.9937	y = 6.737x + 46.44 R^2 = 0.8403	y = 23.009x + 196.97 R^2 = 0.9715	y = 4.349x + 5.89 R^2 = 0.9797	y = -4.087x - 17.409 R^2 = 0.9188
TI4	y = -299.05x + 319.32 R^2 = 0.935	y = -91.28x + 87.312 R^2 = 0.9402	y = -143.72x + 177.68 R^2 = 0.6684	y = -515.7x + 658.2 R^2 = 0.8530	y = -100.32x + 94.565 R^2 = 0.9109	y = 99.834x - 103.65 R^2 = 0.9583
TI5	y = 5.171x + 104.89 R^2 = 0.6186	y = 1.625x + 21.339 R^2 = 0.6594	y = 1.88x + 81.385 R^2 = 0.253	y = 8.609x + 291.88 R^2 = 0.5259	y = 1.779x + 22.138 R^2 = 0.6338	y = -1.896x - 30.165 R^2 = 0.7651
TI6	y = -133.7x + 338.61 R^2 = 0.058	y = -48.873x + 103.81 R^2 = 0.0836	y = 26.132x + 67.983 R^2 = 0.0069	y = -200.53x + 651.93 R^2 = 0.04	y = -53.424x + 112.32 R^2 = 0.0801	y = 74.098x - 148.86 R^2 = 0.1637

Aiming for better correlations we have tested bilinear relationships relating molecular properties with pairs of LOEI based TIs. Figure 5 displays the graphs and correlation coefficients for molar volume, where TI_1 and TI_5 or TI_1 and TI_6 were used as independent variables in the analysis. The bilinear equations used to obtain calculated MV values are:

a) $MV_{calc} = 56.237249+24.654136*TI_1–2.043641*TI_5$

b) $MV_{calc} = 20.53857+90.28144*TI_1–63.83*TI_6$



a) b)

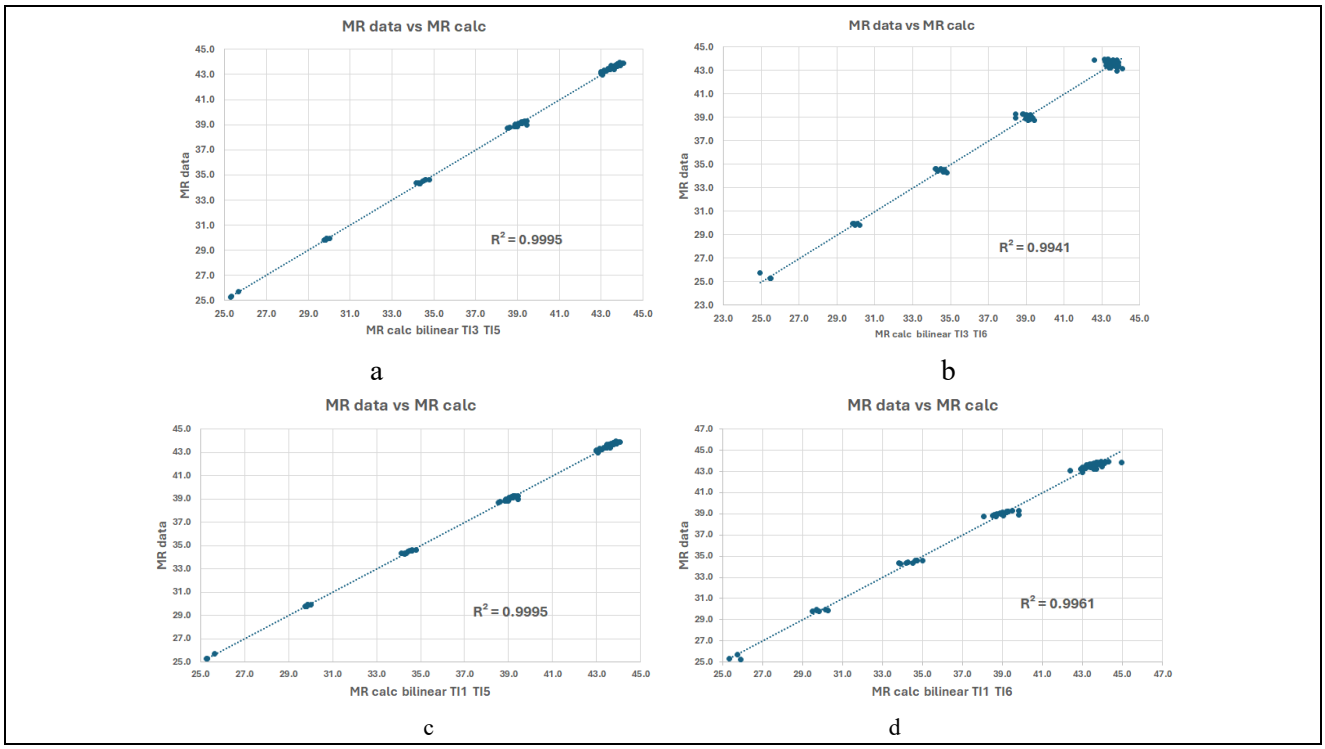
Fig. 5 – Experimental *vs* calculated molar volume (MV). Calculated values obtained with bilinear regression using TI_1 and TI_5 or TI_1 and TI_6 as independent variables.

Figure 6 displays the graphs and correlation coefficients for molar refraction, where the pairs TI_3–TI_5, TI_3–TI_6, TI_1–TI_5 and TI_1–TI_6 were used as independent variables in the analysis. In this case adding a second independent variable does not improve in a significant way the correlation, which was already very good: R^2=0.9937 using TI_3 alone. The bilinear equations used to generate data represented in Fig. 6 are:

a) $MR_{calc} = 7.159826+3.696552*TI_3+0.1466*TI_5$
b) $MR_{calc} = 11.84076+3.90067*TI_3–3.60057*TI_6$
c) $MR_{calc} = 7.0913972+7.2192781*TI_1–0.487522*TI_5$
d) $MR_{calc} = –17.6596+6.19914*TI_1+18.73285*TI_6$

In the case of boiling points using pairs of LOEI based TIs do not improve significantly the quality of the correlation but a significant improvement can be reached using as a second independent variable a local vertex invariant based TI. Such TIs can be obtained as presented in our previous work.[13] In this case we built the system of linear equations starting from the adjacency matrix of the molecular graph using atomic number (Z) as diagonal terms and the degree of vertices as free terms. Solving the system, we obtain LOVIs and summing them up we obtain the TI_{lovi} used in the bilinear correlation of boiling points. The graph from the right side of Fig. 7 shows the correlation of experimental boiling points for C5–C9 alkanes with the ones calculated with the following bilinear equation:

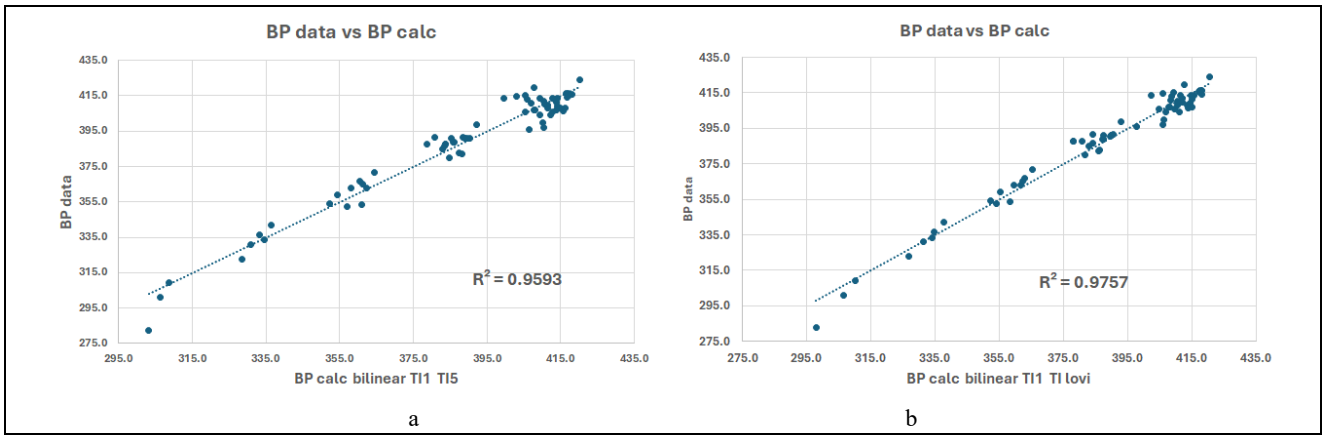
a) $BP_{calc} = 196.4712+48.34166*TI_1–5.538659*TI_5$
b) $BP_{calc} = 197.5745+6.772469*TI_1+90.73559*TI_{lovi}$



a b

c d

Fig. 6 – Experimental *vs* calculated molar refraction (MR). Calculated values obtained with bilinear regression using pairs TI_3–TI_5, TI_3–TI_6, TI_1–TI_5 and TI_1–TI_6 as independent variables.



a b

Fig. 7 – Experimental *vs* calculated boiling points (BP). Calculated values were obtained with bilinear regression using TI_1 and TI_5 or TI_1 and TI_{lovi} as independent variables.

For entropy and heat capacity good bilinear correlation has been obtained using the TI1–TI5 and TI1–TI_{lovi} pairs respectively. Results are shown in Fig. 8. The bilinear equations used to obtain calculated E and Cp values are:

a) $E_{calc} = 56.237249+24.654136*TI_1–2.043641*TI_5$

b) $Cp_{calc} = 20.53857+90.28144*TI_1–63.83*TI_6$

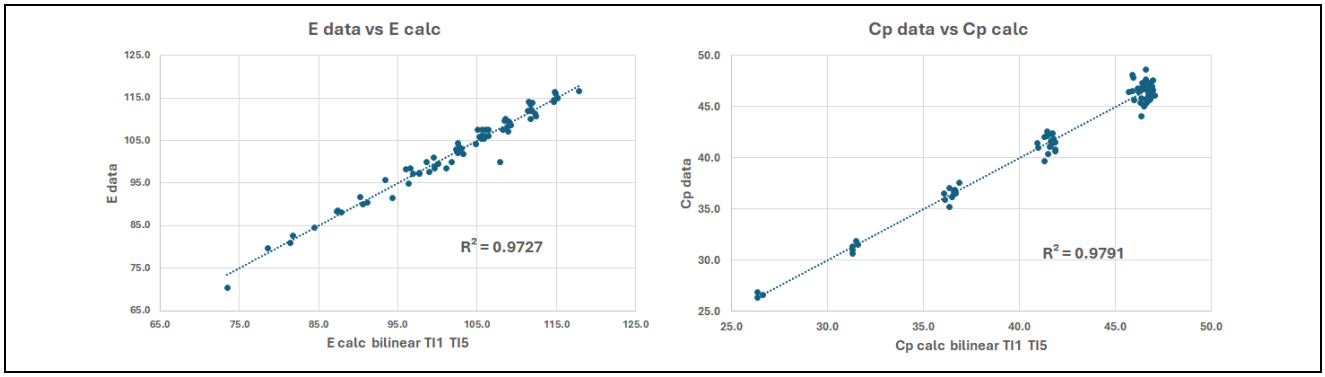
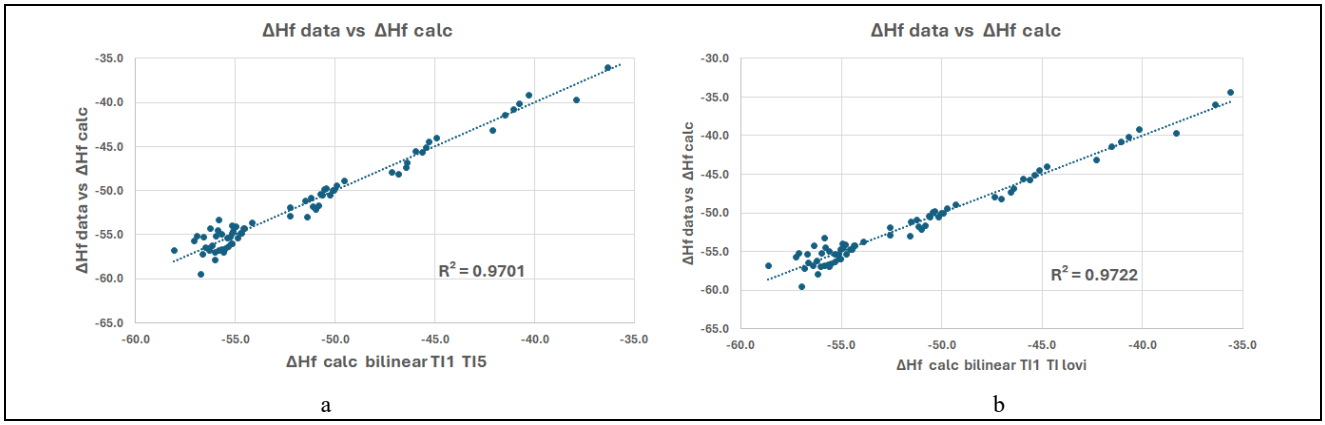


Fig. 8 – Experimental vs calculated for entropy (E) and heat capacity (Cp). Calculated values were obtained with bilinear regression using as independent variables TI_1 and TI_5 for E and TI_1 and TI_{lovi} for Cp.

In the case of enthalpy of formation adding a second independent variable, at least the TIs we used in this study, does not improve significantly the quality of correlation: $R^2 = 0.9694$ for TI_1 as independent variable and 0.9701 for the bilinear equations using TI_1 and TI_5 and 0.9722 when TI_1 is used together with TI_{lovi}.



a b

Fig. 9– Experimental vs calculated for enthalpy of formation (ΔHf). Calculated values were obtained with bilinear regression using as independent variables the pairs TI_1–TI_5 and TI_1–TI_{lovi}.

CONCLUSIONS

New third generation topological indices have been defined based on the edge adjacency matrix connected to a molecular graph. A system of linear equations is built, as shown in Fig. 2, using bond properties as diagonal terms in the edge adjacency matrix and as free terms of the equations. Solving the system local bond invariants (LOEI), which respect the symmetry of the molecule, are obtained and using the formulas presented in Table 1 topological indices TI_1–TI_6 are generated. This TIs have been further used in QSPR studies relating them to molecular properties of C5–C9 alkanes. Good correlations have been obtained for molar volume, molar refraction and thermodynamic properties in linear correlations with single TIs and in some cases better ones using bilinear equations using pairs of TIs as independent variables.

REFERENCES

1. T. Balaban, *J. Chem. InJ Compur. Sci.* **1985**, *25,* 334–343.
2. A. Todeschini and V. Consonni, “Molecular Descriptors for Chemoinformatics”, 2 volumes, Wiley-VCH Verlag GmbH, Weinheim, Germany, 2009.
3. A. Hansch, P. Maloney, T. Fujita and R. Muir, *Nature* **1962**, *194*, 178−180.
4. A. Crum-Brown and T. R. Fraser, *Transactions of the Royal Society of Edinburgh*, **1886**, *25*,151–203, doi:10.1017/S0080456800028155 PMID:17230757
5. J. Devillers and A. T. Balaban, “Topological Indices and Related Descriptors in QSAR and QSPR”, CRC Press, 2000.
6. R. Todeschini and V. Consonni, MATCH *Commun. Math. Comput. Chem.*, 2010, *64*, 359–372.
7. O. Ivanciuc, *J. Chem. Inf. Comput. Sci*., **1997**, *37*, 405–406.
8. A. Mauri, V. Consonni, M. Pavan and R. Todeschini*, MATCH Commun. Math. Comput. Chem*., **2006**, *56*, 237–248.
9. H. Moriwaki, Yu-Shi Tian, N. Kawashita and T. Takagi, *J. Cheminform.*, **2018***, 10*, 4, doi: 10.1186/s13321-018-0258-y
10. W. Yap, *J. Comput. Chem*., **2011**, *32*, 1466–1474.
11. L. Tarko, I. Lupescu and D. Groposila-Constantinescu, *ARKIVOC*, **2005,** *x*, 254–271.
12. A. T. Balaban, *J. Chem. Inf. Compur. Sci.*, **1992**, *32*, 23–28.
13. P. A. Filip, T. S. Balaban and A. T. Balaban, *J. Math.Chem.*, **1987**, *1*, 61.
14. Janežič, S. Nikolić, A. Miličević and N. Trinajstić "Graph theoretical matrices in chemistry", I. Gutman (Ed.), “Mathematical chemistry monographs 3”, University of Kragujevac, Serbia, 2007, p. 27.
15. Gutman and E. Estrada, *J. Chem. Inf. Comput. Sci.*, **1996,** *36,* 541–543.
16. Estrada, *J. Chem. In& Comput. Sci.*, **1995**, *35,* 31–33.
17. A. Miličević, S. Nikolić and N. Trinajstić, *Mol. Diversity*, **2004**, *8***,** 393–399.
18. X.-L. Peng, K.-T. Fang, Q.-N. Hu and Y.-Z. Liang, *Molecules,* **2004**, *9***,** 1089–1099.
19. Gutman and E. Estrada, *J. Chem. Inf. Comput. Sci*., **1996**, *36***,** 541–543.
20. D. W. Scott, “Chemical thermodynamic properties of hydrocarbons and related substances: properties of the alkane hydrocarbons, C1 through C10, in ideal gas state from 0 to 1500K”, Washington, U.S. Bureau of Mines, 1974.