WIENER INDEX FOR 1-PENTAGON FULLERENIC INFINITE LATTICE

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It will be shown how by using a pure topological approach to the *Wiener index* W one is able to arrive to a suitable topological lattice descriptor for the infinite fullerene fragments (fullerenic graph) that grow around a single pentagonal face by adding an increasing number f of concentric circles made of hexagons. We computed W of such infinite lattices and the results parallel those of Bonchev and Mekenyan[1] who, in studying graphs of polymers with N vertices, discovered a polynomial relationship between W(N) and N. For fullerenic graphs we similarly found the polynomial dependence, W = W(f), of W on the number f. Extracting the minimum contribution to W(f) coming from a given vertex, we demonstrate an interesting feature that this vertex is able to migrate as f increases. All considerations are made in the dual space lattice.

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MOLECULAR MODELLING OF
BISPHENANTHRIDINIUM-NUCLEOBASE CONJUGATES

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We shall present our molecular modelling results in combination with the spectroscopic measurements for a series of nucleobase conjugates of bisphenanthridinium as well as their non-covalent complexes with UMP and AMP. AMBER ff03[1] and GAFF[2] force fields were used to parameterize molecules and Molecular Dynamics (MD) simulations were accomplished with the program AMBER9[2]. The simulations were performed in explicit water (TIP3P water type) using periodic boundary conditions. The maximally folded conformers (with rings stacked) were used as the starting ones. During the MD simulations conformation of the molecules relaxed; however majority of molecules remained in their folded, more or less stacked conformation with no water molecules accommodated within the two phenanthridinium rings. The most populated conformation of one of the conjugates (S21) in complex with UMP is shown in the Figure 1.
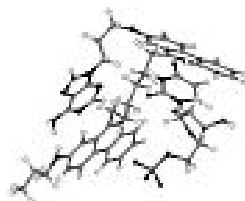

Figure 1. Complex between S21 and UMP

The initial structure of the complex between S21 and UMP was built in a way to enable adenine from S21 and uracil from UMP to form the Watson-Crick type of H-bonds. These H-bonds were preserved during the geometry optimization. However, during the MD simulation the conformation of the complex changed and stabilized in a conformation with adenine in the stacking interaction with one phenanthridinium ring, and uracil with the other. In this interaction the hydrophobic pocket made by two phenanthridinium rings and the alkyl linker is very functional since there is no water molecule within it to compete with uracil from UMP for the hydrogen bond. This result is in accord with the spectroscopic measurements and the high binding affinity of S21 toward UMP.

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COMPARISON OF VARIABLE SELECTION METHODS. PREDICTION OF TOXICITY OF SUBSTITUTED BENZENES

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Variable selection is the key step in modeling, and searching quantitative structure – activity relationships. In the first period, cross-validation and especially leave-one-out procedure (LOO) was accepted as a suitable method for validation. Later, the scientific community agreed in using external validation, i.e. in testing the model performance on an independent prediction set.[1,2] *Independent* here means that this test should not be connected to variable selection, model building, parameter estimation, determining latent variables and similar steps. However, recent and extensive examinations have shown that LOO is much better than previously thought.[3]

Hence, our aim was to study and to compare various modeling and especially variable selection methods. A well-known data set has been chosen for comparison.[4,5]

Our results indicate that

(*i*) the split into three sets is too conservative;

(*ii*) the leave-one-out is not biased more than external validation;

(*iii*) PLS (without any variable selection) successfully competes with the best variable selection methods;

(*iv*) ordering of variable selection methods: CromRSel > FS > mBSS ~ PLS ….;

(*v*) it is worth to filter out the outliers (even from among the tests set);

(*vi*) PCM and Marten's test provides comparable results;

(*vii*) consensus modeling of the four best methods overcomes the best performance for any individual model on the entire data set!

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QSAR OF 1,4-BENZOXAZIN-2,3- AND 3,1-BENZOXAZIN-2,4-DIONE ANTIMICROBIAL ANALOGUES

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Recently, different benzoxazindione analogues were investigated for their antiviral, antiallergic and tocolytic oxytocin receptor activities. The benzoxazinone analogue efavirenz, *i.e.,* 6-chloro-4-(cyclopropylethynyl)-1,4-dihydro-4-(trifluoromethyl)-2H-3,1-benzoxazin-2-one, was approved as antiretroviral drug, a non-nucleoside type of reverse transcriptase inhibitor.

In extension of our previous QSAR studies using topological indices, TIs (W, χ^1, J), the QSAR of 1,4-benzoxazin-2,3-dione and 3,1-benzoxazin-2,4-dione analogues were explored using different computed molecular descriptors (MDs) and experimentally obtained parameters for antimicrobial activity (MIC).

The biological activities were evaluated using G(+) and G(-) test bacteria and *Candida monosa*. In this study additional TIs and other MDs were explored (CID, χ^1, χMOD, VRA1, BID, Sv, Se and ALOGP) using multiple linear regression analysis.

Previous results have shown significant correlation between antimicrobial activity (MIC) and topological indices (TIs), while in present, which are in good agreement with previously obtained, correlations indicate the preference of biological predictability on the basis of two or more TIs. This approach allows an investigation of influences of more than one descriptor on particular system such as combination of constitutional (Sv, Se,...), topological (ISIZ, MV1,…), and molecular properties (ALOGP, MLOGP) descriptors.

The good correlation was observed between constitutional (Sv) and topological (ZM1V) descriptors and antimicrobial activity (MIC) towards *Klebsiella pneumoniae*.

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QSAR OF 1,4-BENZOXAZIN-2,3- AND 3,1-BENZOXAZIN-2,4-DIONE ANTIMICROBIAL ANALOGUES

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WHY DOES ANHYDROUS BIS(L-VALINATO)COPPER(II) CRYSTALLISE AS A *TRANS*-ISOMER? MOLECULAR MECHANICS CALCULATIONS IN SIMULATED CRYSTAL LATTICE

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Bis(amino acidato)copper(II) complexes are biologically important compounds. They take part in transporting copper to copper enzymes (such as superoxide dismutase, cytochrome c oxidase and nitrous-oxide reductase) and electron-transfer copper proteins (e.g. plastocyanin, azurin). The X-ray crystal structures are the most common source of experimental information on the structural properties of this class of compounds.

Bis(L-valinato)copper(II), Cu(L-Val)$_2$, after being heated in a dryer for 24 hours at 80 °C crystallised from aqueous solution as anhydrous *trans*-isomer (space group P1) as determined by the X-ray diffraction measurements.[1] If not heated, it crystallised as a *cis*-isomer with one water molecule in the asymmetric unit.[1] The coordination geometry of the copper(II) in the anhydrous modification is a distorted planar. The crystal structure contains polymeric chains that are made up of complex dimers that are formed by interlinkage of adjacent molecules *via* axial copper(II)-to-carbonyl oxygen contacts, and are further stabilised by N–H···O hydrogen bonds.

Molecular mechanics force field FFW,[2] developed for studying the properties of anhydrous and aqua bis(amino acidato)copper(II) complexes with either *cis*- or *trans*-N$_2$O$_2$ copper(II) coordination geometry in the solid state and *in vacuo,* was used for conformational analysis of the title compound.

Each chelate ring of Cu(L-Val)$_2$ can have 6 conformations, with C$^\beta$ in 3 axial and 3 equatorial positions, and therefore the molecule can have 21 *trans* and 21 *cis* conformations. Conformational analysis *in vacuo*, without the influence of the intermolecular interactions, showed that the *trans* conformers were more stable than the *cis* ones (by $\approx$ 21.3 kcal mol^{-1}). To account the crystal lattice effects, the geometry optimisations of all possible conformers were attained by taking the experimental molecule orientation, unit cell lengths and angles, as well as the P1 space group symmetry operations as the starting input data. During the energy minimisation of a crystal all degrees of freedom were allowed to vary. The calculations of the unit cell packings and intermolecular interactions for the series of conformers suggest the reasons why experimentally obtained conformer occurs in the real crystal structure.

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INSIGHT INTO THE DEPENDENCE OF STABILITY ON ALKYLATION POSITION IN COPPER(II) DIETHYLENETRIAMINE COMPLEX *via* VALENCE CONNECTIVITY INDEX

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Valence connectivity index $^3\chi^v$ was correlated to the log K_1 of copper(II) complexes with diethylenetriamines (CuL, N = 8). In spite of very high correlation coefficient, r = 0.965, standard error obtained by the leave-one-out procedure of cross validation (*cv*) was unsatisfactory, $S.E._{cv}$ = 0.62.[1] However, the regression strongly indicates discrepancy in stability of two subsets of the diethylenetriamine complexes. Namely, influence of the middle nitrogen atom alkylation on the stability constant differs from the influence of alkylation at the terminal nitrogens.[2] Moreover, the protonation constant of the middle nitrogen is several orders of magnitude lower than the protonation constants of terminal nitrogens. Thereby, we introduced an indicator variable (*In*) into the regression; *In* = 1, for triamine complex alkylated at the middle nitrogen, and *In* = 0 for the complexes with alkyl substituents only at the terminal nitrogens. This resulted in much better (bivariate) regression, r = 0.998 and $S.E._{cv}$ = 0.16.

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THE RELATIONSHIPS BETWEEN THE π–ELECTRON ENERGIES AND CONNECTIVITY INDICES OF POLYCYCLIC CONJUGATED HYDROCARBONS REVISITED

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The relationship between the π-electron energies (E_π) and standard (χ) and valence (χ^v) connectivity indices of selected benzenoid and non-benzenoid hydrocarbons is revisited. The initial on the relationship between E_π and χ and χ^v for polycyclic conjugated hydrocarbons appeared in Refs. 1-3. The following results are found in the revision:

(*I*) For 30 lowest benzenoid hydrocarbons the following relationship between E_π and χ is found: $E_\pi = 2.944 \ (\pm 0.022) \ \chi$ - $1.081 \ (\pm 0.223)$ (R = 0.9992, S = 0.272, R_{cv} = 0.9990, S_{cv} = 0.318, F = 18379.40)

(*II*) For 30 lowest non-benzenoid hydrocarbons the following relationship between E_π and χ is found: $E_\pi = 2.899 \ (\pm 0.048) \ \chi$ - $1.151 \ (\pm \ 0.293)$; (R = 0.9961, S = 0. 460, R_{cv} = 0.9955, S_{cv} = 0.500, F = 3610.78)

(*III*) For all considered benzenoid and non-benzenoid hydrocarbons the following relationship between E_π and χ is found: $E_\pi = 2.974 \ (\pm 0.018) \ \chi$ - $1.486 \ (\pm 0.151)$; (R = 0.9989, S = 0.406, R_{cv} = 0.9989, S_{cv} = 0.423, F = 27408.93)

(*IV*) For 30 lowest benzenoid hydrocarbons the following relationship between E_π and χ^v is found: $E_\pi = 4.085 \ (\pm 0.016) \ \chi^v$ - $0.271 \ (\pm 0.113)$; (R = 0.9998, S = 0.142, R_{cv} = 0.9997, S_{cv} = 0.160, F = 67203.11)

(*V*) For 30 lowest non-benzenoid hydrocarbons the following relationship between E_π and χ^v is found: $E_\pi = 4.088 \ (\pm 0.049) \ \chi^v$ - $0.709 \ (\pm 0.206)$; (R = 0.9980, S = 0.332, R_{cv} = 0.9976, S_{cv} = 0.365, F = 6973.05)

(*VI*) For all considered benzenoid and non-benzenoid hydrocarbons the following relationship between E_π and χ^v is found: $E_\pi = 4.156 \ (\pm 0.018) \ \chi^v$ - $0.874 \ (\pm 0.108)$; (R = 0.9994, S = 0.296, R_{cv} = 0.9994, S_{cv} = 0.308, F = 51502.14)

From the above results, it appears that valence connectivity indeks produces a bit better correlation with π-electron energies of polycyclic conjugated hydrocarbons.

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ANALYSIS OF SUMMER 2006 OZONE POLLUTION IN ZAGREB

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Zagreb, the capital of Croatia, has one of the longest history of surface ozone measurements in Europe. Early measurements have been done from 1889 – 1900 by Andrija Mohorovičić,[1] the discoverer of the Moho layer (discontinuity in Earth`s mantle), who used Schönbein's method. In the 20th century measurements performed in 1975 in the city centre at 110 m a.s.l. indicated that within that time gap ozone concentration in Zagreb must at least have doubled.[2] A statistical analysis of the later data which showed pronounced diurnal variation based on correlation with meteorological variables also connected particularly high ozone values with slow SE wind, *i.e.*, transport from the city`s industrial and airport site.[3] Later ozone measurements performed at the elevated RBI station (180 m a.s.l., the Ruđer Bošković Institute) in residential northern part of Zagreb revealed much less influence of these high ozone levels produced in the south. Measurements at the stations Medvedgrad and Puntijarka at 580 m and 980 m a.s.l., respectively, on the mountain Medvednica north above Zagreb also showed that the inversion layer rarely reaches 500 m and never 980 m.[4,5] Therefore, the latter has been chosen as an EUROTRAC-TOR station[6] to represent the regional free atmosphere in the corresponding network of stations from 1989-2002. Measurements are still being continued there. Here we report an effort to investigate for summer 2006 the dependence of ozone production, destruction and transport at three same elevation sites located along the 15 km S – N line on equidistant stations Velika Gorica (VG), Dugave (DUG) and Institute for Medical Research and Occupational Health (IMI) stretching from Zagreb Airport to about 2.5 km north from the city center where the station IMI is located.

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GROWING LARGER NUT FULLERENES

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A molecular graph has a non-bonding molecular orbital (NBMO), if zero is an eigenvalue of its adjacency matrix. This follows from the Hückel Molecular Orbital (HMO) model, approximating the distribution of the π-electrons in unsaturated organic molecules, as a solution of the Schrödinger equation. A nut graph has one NBMO of the π-electron occupying this orbital and each entry of the associated (kernel) eigenvector is non-zero. In chemistry, this is significant. In the radical molecule that would have the NBMO as partially occupied HOMO, all centres carry non-zero spin density. The charge, spin and bond-order densities of a π-electron, occupying the NBMO, is distributed over the whole structure and not on some substructure. Thus all C-centres are likely to be involved in reactions. There are only 41 nut fullerenes on up to 120 vertices, but these can be grown into larger ones by coalescence, that is the identification of a C center on two distinct nut fullerenes. Besides, a nut fullerene can be coalesced with molecules, other than nut graphs, to produce larger structures with a concentrated area where a NBMO has non-zero entries. Moreover, local enlargements for trivalent polyhedra, cylindrical constructions of nut fullerenes, as well as an extension to four-valent polyhedra are proposed.

Key words: NBMO, adjacency matrix, nut fullerenes, kernel eigenvector, coalescence, local enlargement

ON FRIES AND CLAR STRUCTURES IN PREDICTING RESONANCE ENERGIES OF BENZENOIDS

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We investigated benzenoids with five, six and seven rings. A correlation between resonance energies DRE and TRE and number of Kekulé structures in these molecules has been studied. We tried to improve the correlation by taking also into account Fries and Clar structures.

OPTIMIZATION PROCEDURE TO DETECT HIGH-AFFINITY LIGAND-RECEPTOR AMINO ACID PAIRS

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We describe the procedure for detecting the most probable ligand-receptor amino acid pairs. The method is suitable for investigating epitope-paratope interactions. The procedure is based on the combination of methods from the Molecular Recognition Theory and algorithms for the prediction of protein secondary structure. The results are tested on the molecular models of CD20, PSA, α-melanotropin and Newcastle virus surface proteins.