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Idealized correlations: prediction of solubility of fullerene in organic solvents

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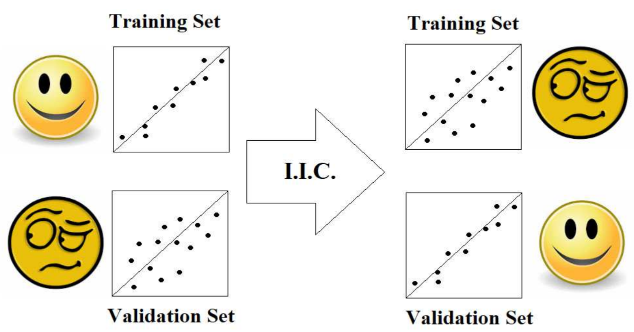
Graphical Abstract



Abstract.
The idealization of correlation is reached via so-called Index of Ideality of Correlation (*IIC*). The *IIC* is a mathematical function of two parameters (i) determination coefficient; and (ii) mean absolute error (MAE). Optimal descriptors, which are calculated with simplified molecular input-line entry system (SMILES), obtained via the Monte Carlo optimization that involves the *IIC* factually have lost ability to provide the overtraining for quantitative structure - property relationships (QSPRs).

Introduction

Physicochemical properties of nanomaterials is important information for chemical industry, biochemistry, and medicine. Solution of fullerene in any solvent factually is a Nano-object. Consequently, the development of predictive models for solubility of fullerene in organic solvents is an actual task of modern natural sciences as well as an actual task of nanotechnology [1-5].

The Index of Ideality of Correlation (*IIC*) has been suggested recently as a tool to improve predictive potential for quantitative structure – property / activity relationships (QSPRs/QSARs) [6, 7]. The aim of the present study to compare the QSPR models for fullerene solubility in different solvents, which are obtained with applying of the *IIC* and models obtained without *IIC*.

Materials and Methods

Data.

The experimental data on the fullerene solubility (logS) are taken in the literature [8]. Four solvents have undefined values (logS<-8). These solvents were removed from consideration, consequently 128 solvents are examined here. The total data (n=128) were randomly split into the training, invisible training, calibration, and validation sets. Each set has special task:

1. The training set is 'builder' of the model. Compounds from this set are basis to obtain the correlation weights, which give maximal value of target function;
2. The invisible training set is inspector' of the model. Compounds of this set are basis to check up: whether the model is satisfactory for substances, which are not involved into the Monte Carlo optimization;
3. The calibration set is 'estimator' of the model; and the task of this set is to detect start of the overtraining; and
4. Finally, there is the validation set: these substances are the basis of final checking up of the predictive potential of the model.

Optimal descriptor

The optimal descriptor is a mathematical function of simplified molecular input line-entry system (SMILES) [10]. The SMILES contains a group of SMILES-atom. The SMILES-atom can be one character or two characters, which cannot be examined separately (e.g. 'Cl', 'Br', etc.).

$$DCW(T^*,N^*) = \sum_{k=1}^{NA} CW(S_k) + \sum_{k=1}^{NA-1} CW(SS_k) \qquad (1)$$

The descriptor is calculated with so-called correlation weights, i.e. coefficients which calculated by the Monte Carlo method by algorithm described below. The Sk is the SMILES-atom. The SSk is a pair of SMILES atoms which are neighbors in the SMILES notation. The NA is the number of SMILES-atoms for a given SMILES [9]. The Sk and SSk are SMILES attributes. The Monte Carlo method gives model that is one variable correlation:

$$Solubility\ C60 = C_0 + C_1 \times DCW(T^*,N^*) \qquad (2)$$

The $CW(S_k)$ and $CW(SS_k)$ are the above-mentioned correlation weights for the above-mentioned SMILES-attributes. The correlation weights are special coefficient calculated with the Monte Carlo method. The numerical data on the correlation weights should provide maximal value of a target function (*TF*) calculated as the following:

$$TF = R_{training} + R_{invisible-training} - \left|R_{training} + R_{invisible-training}\right| \times 0.1 \qquad (3)$$

Recently, the modified target function that improves QSPR/QSAR models based on the traditional correlation has been suggested. The Index of Ideality of Correlation (*IIC*) [9] is additional component of the function:

$$TF_m = TF + IIC \times 0.1 \qquad (4)$$

The *IIC* can be qualified as a criterion to estimate statistical quality of a model. The scheme to calculate *IIC* is the following.

$$delta_k = observed_k - calculated_k \qquad (5)$$

The $observed_k$ and $calculated_k$ are values of an endpoint.

Having data on all $delta_k$ for the calibration set, one can calculate sum of negative and positive values of $delta_k$ similar to mean absolute error (MAE):

$$^{-}MAE_{calibration} = \frac{1}{^{-}N}\sum_{k=1}^{^{-}N}|delta_k| \quad delta_k < 0,\ ^{-}N \text{ is the number of } delta_k < 0 \tag{6}$$

$$^{+}MAE_{calibration} = \frac{1}{^{+}N}\sum_{k=1}^{^{+}N}|delta_k| \quad delta_k \geq 0,\ ^{+}N \text{ is the number of } delta_k \geq 0 \tag{7}$$

$$IIC = r_{calibration} \times \frac{\min(^{-}MAE_{calibration}, ^{+}MAE_{calibration})}{\max(^{-}MAE_{calibration}, ^{+}MAE_{calibration})} \tag{8}$$

The *IIC* can be calculated for training, invisible training, and validation sets, but the key role for the index is improving of the predictive potential of a model is related to the calibration set.
The *T* is threshold to discriminate SMILES-atoms into two classes (i) rare, which is noise and should be removed from building up a model; and (ii) not rare, which are basis to build up the model. The *N* is the number of epochs of the Monte Carlo optimization. The *T*=*T** and *N*=*N** are values of the parameters which gives the best results for the calibration set.

Results and Discussion

Table 1 contains statistical quality of models for fullerene solubility build up with target function TF calculated with Eq. 3 and TFm calculated with Eq. 4. Factually, data from Table 1 confirms that the IIC improves the predictive potential of the model for fullerene solubility. The similar situation was described for models of mutagenicity [6] and for models of skin permeability [7].
The statistical quality of prediction for the model of solubility of fullerene in organic solvents that is suggested in the literature [8] is the following: n=28, r^2=0.804, RMSE=0.386. In other words, models (obtained with applying the *IIC*) represented in Table 1 have comparable, or even better, predictive potential.

[Table 1 around here]

Conclusions

The applying of the *IIC* as addition component of the target function for the Monte Carlo optimization is considerable improves the predictive potential of the model based on the optimal SMILES-based descriptors calculated with the CORAL software (http://www.insilico.eu/coral).

Acknowledgments

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Table 4

Statistical characteristics of models for solubility of fullerene C60 in different solvents

Split	*Target function*	Set	n*	r^2	*IIC*	CCC	Q^2	RMSE
#1	*TF*	Training	33	0.9022		0.9486	0.8932	0.385
		Invisible training	32	0.8306		0.8763	0.8108	0.677
		Calibration	32	0.7771	0.6376	0.8094	0.7513	0.658
		Validation	31	0.8231				0.507
	TF_m	Training	33	0.7550		0.8604	0.7206	0.610
		Invisible training	32	0.7577		0.8348	0.7246	0.731
		Calibration	32	0.8671	**0.7465**	0.9166	0.8482	0.357
		Validation	31	**0.8280**				**0.356**
#2	*TF*	Training	32	0.8435		0.9151	0.8284	0.450
		Invisible training	32	0.8400		0.8458	0.8235	0.697
		Calibration	33	0.7471	0.6343	0.8588	0.7071	0.462
		Validation	31	0.8436				0.396
	TF_m	Training	32	0.8195		0.9008	0.7980	0.484
		Invisible training	32	0.7548		0.8534	0.7281	0.734
		Calibration	33	0.8306	**0.8009**	0.9110	0.7917	0.387
		Validation	31	**0.8713**				**0.348**
#3	*TF*	Training	31	0.8429		0.9148	0.8219	0.553
		Invisible training	32	0.8401		0.6400	0.8150	0.801
		Calibration	32	0.6632	0.4648	0.8129	0.6250	0.624
		Validation	33	0.7725				0.618
	TF_m	Training	31	0.8140		0.8975	0.7888	0.601
		Invisible training	32	0.7062		0.6998	0.6474	0.768
		Calibration	32	0.8613	**0.7727**	0.9243	0.8367	0.383
		Validation	33	**0.8810**				**0.410**

*) n = the number of solvents in a set; r^2 = determination coefficient; CCC = concordance correlation coefficient; q^2 = cross validated determination coefficient; RMSE = root mean squared error. Best models are indicated by bold.