Understanding odour thresholds: A Quantitative Structure-Property Relationship study of the role of the molecular structure

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UNDERSTANDING ODOUR THRESHOLDS:
A QUANTITATIVE STRUCTURE-PROPERTY RELATIONSHIP (QSPR) STUDY OF THE ROLE OF THE MOLECULAR STRUCTURE

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THRESHOLDS ARE USEFUL

- They are commonly used in food science to evaluate the **potency** of an aroma compound, which varies from one compound to another.
- This characteristic is usually associated with the molecule's **odour detection threshold** (ODT).
- However, the relationship between a **molecule's structure** and its ODT has not a straightforward answer.

WE HAD SOME QUESTIONS...

- What is the role of the **chemical structure** on odour detection thresholds?
- What are the most impactful **molecular descriptors** representing these chemical features?

DATA TREATMENT AND MODELLING

ODT values in water from the literature
- 33 research papers
- 407 molecules
- 858 ODT values

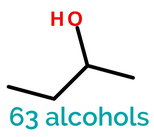
→ **Removal of outliers**: Z-test

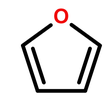
→ Average ODT for each molecule

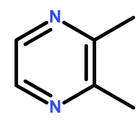
→ **Calculation of molecular descriptors**: >5,000 descriptors, Biovia Discovery Studio

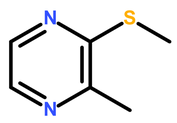
Model development
- Generation of QSPR models by Genetic Functional Analysis (GFA)
- Multiple linear equations for the correlation of ODT values (dependent variable) and molecular descriptors (independent variables)
- Optimisation by maximisation of R^2
- A balance between the number of descriptors and the model fit is preferred, i.e. the best fit for the fewer variables.

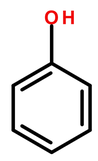
The **407 aroma** compounds employed belong to a large variety of chemical classes with a large variety of functional groups.

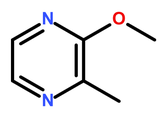

63 alcohols

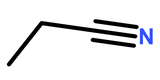

20 furans

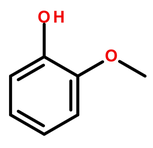

33 pyrazines

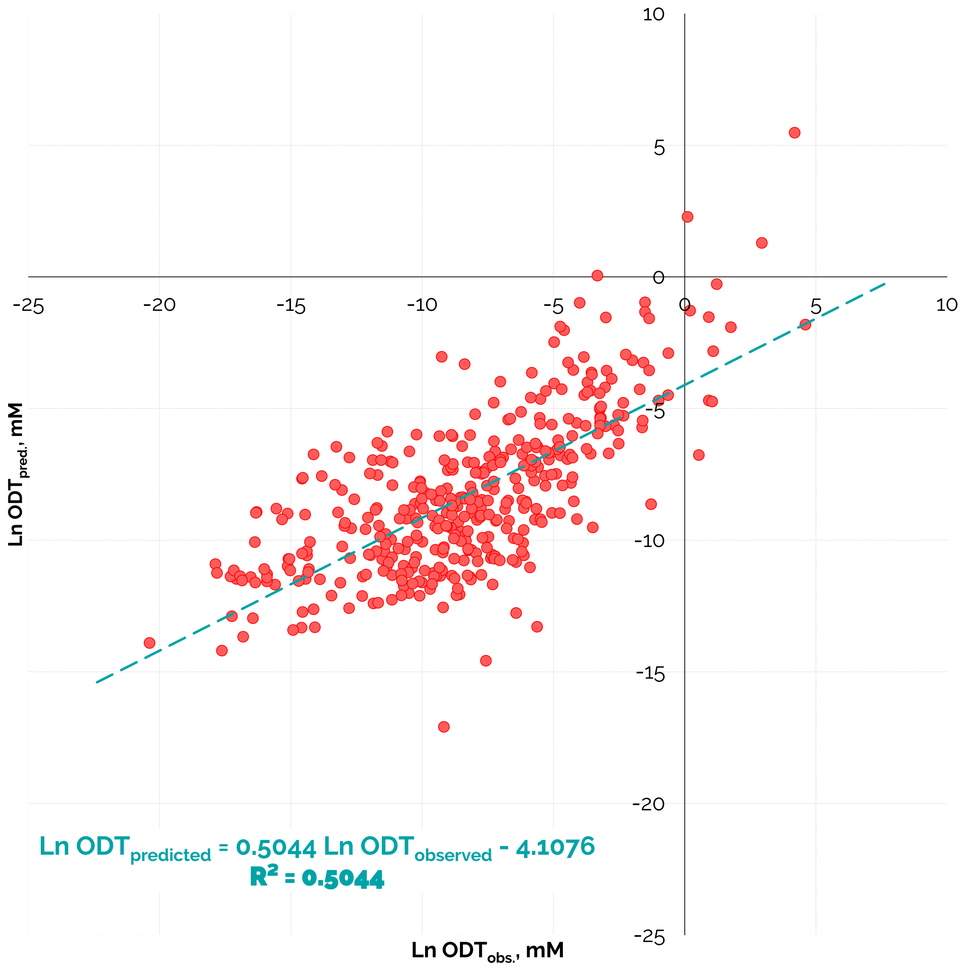

38 sulfanyl pyrazines


8 phenols

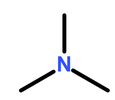

51 alkoxy pyrazines

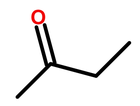

4 nitriles

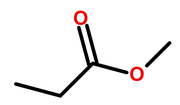

6 methoxyphenols

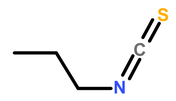


Ln ODT$_{predicted}$ = 0.5044 Ln ODT$_{observed}$ - 4.1076
R^2 = 0.5044

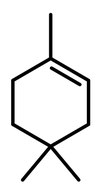

6 amines

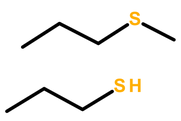

27 ketones

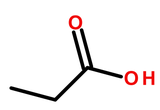

31 esters


5 isothiocyanates


51 aldehydes


9 hydrocarbons


18 sulphides and thiols


16 carboxylic acids

The proposed 6-variable model:

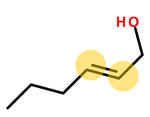
Ln ODT = 16.56 − 0.93 · ES_Count_dsCH − 2.38 · ES_Count_ssO − 11.23 · Jurs_RASA − 0.14 · Jurs_RNCS − 0.12 · Molecular_Weight + 0.015 · V_DIST_equ

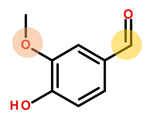
WHAT DO THESE MOLECULAR DESCRIPTORS MEAN?

A molecular descriptor is a structural or physicochemical property of a molecule or a part of a molecule.

ES_Count_dsCH
- Number of =CH- groups in a molecule, i.e. containing a double ('d') and a single ('s') bound (nonaromatic).

ES_Count_ssO
- Number of O atoms bound by two single ('s') bounds (nonaromatic) to atoms other than H.

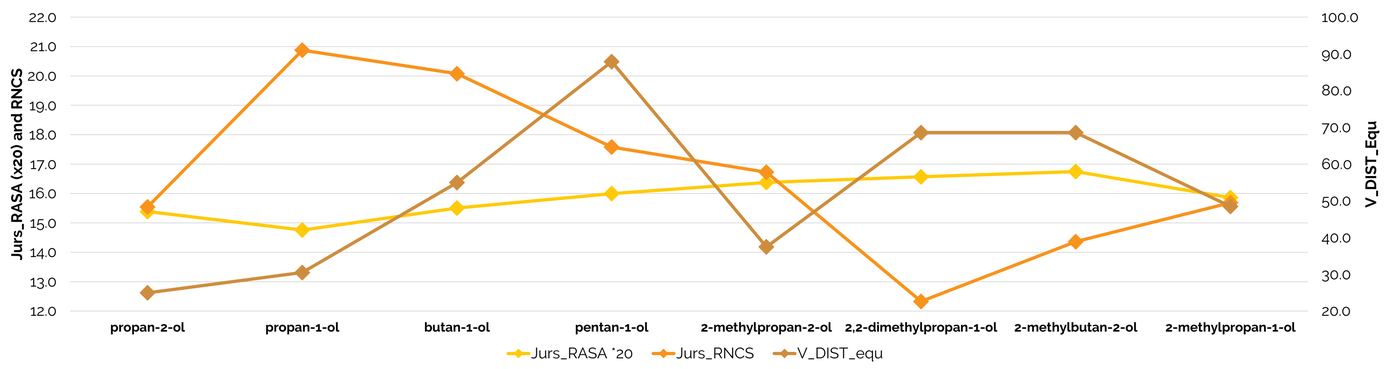

(*E*)-2-hexen-1-ol
ES_Count_dsCH = 2
ES_Count_ssO = 0


vanillin
ES_Count_dsCH = 1
ES_Count_ssO = 1

Jurs_RASA
- Relative Apolar Surface Area. The total hydrophobic surface area (TASA) divided by the total molecular solvent-accessible surface area (SASA).

Jurs_RNCS
- Relative Negative Charged Surface. The solvent-accessible surface area of the most negative atom (SA^-_{max}) divided by the relative negative charge (RNCG).

V_DIST_Equ
- Vertex distance/equality. A descriptor based on a matrix containing information about the distances between the different parts of a molecule.
- Related to the shape of the backbone of the molecules.



- The descriptors associated to hydrophobic features (ES_Count_dsCH and Jurs_RASA), to the size of the molecule (Molecular weight) and its electronegativity (ES_Count_ssO and Jurs_RNCS) contribute negatively to the ODT values.
- Only V_DIST_Equ, also related to size and shape, contributes positively, counterbalancing the weight of the others.
- **The more hydrophobic, heavy/big and/or electronegative, the lower the threshold in water.**

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