CATALYSIS CONSULTING

Principal Component Analysis

Principal Component Analysis (PCA) is a useful statistical technique for identifying patterns in large datasets. PCA will map components expressing the data in such a way as to highlight their similarities and differences.

Mapping will:

- Identify patterns in data
- Identify material with similar properties
  - Even stucturally different
- Provide choices
- Enable effective and efficient progress
- Support informed decision making

PCA mapping can be used for the selection of a range of materials including solvents, aldehydes, amines, chromatography supports, ketones, Lewis acids and even ligands for catalytic reactions. It is important to employ the appropriate descriptors that describe the key principal properties of the reagents for the given experiment to generate the most useful PCA maps. We have extensive experience of developing and using a range of PCA maps.

Solvent maps have been used successfully by us to change the solvent in a reaction to:

- Change the selectivity of a reaction.
- Control or minimise impurities in a process.
- Improve the safety of a process.
- Increase the reaction rates of the desired reaction.
- Reduce the environmental impact of a process.
- Reduce the regulatory burden of a process.
- Selectively crystallise one component over another.
- Support reaction workup and easier isolation.

PCA and Solvent Selection

The use of solvents is fundamental to the practice of chemistry. The systematic and quantitative investigation of the way in which solvents affect a given reaction is not trivial. Frequently the actual mechanism of the solvents influence on a physical or chemical process is unclear. Therefore, the choice of an appropriate or alternative solvent can often be challenging.

The change from one solvent to another often involves significant changes in several of the chemical properties. It is impossible to incrementally change one chemical property while keeping all the others constant as a change in the chemical property results in a change in the molecular properties which affects several of the other chemical properties.

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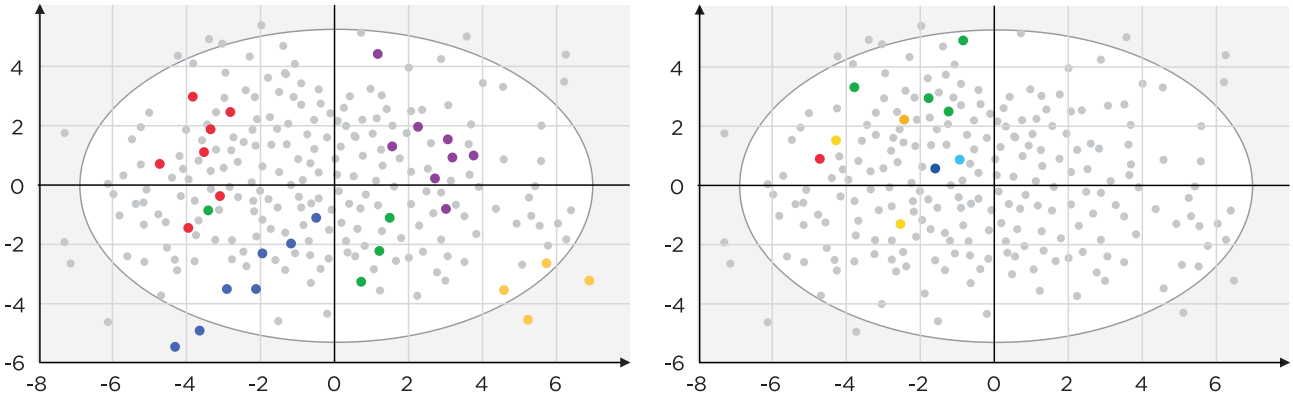
To accurately describe solvents and their influence in chemical reactions, specific measures of their intrinsic molecular properties are required. Previously solvent chemical properties were used as an approximation of molecular properties such as polarity. Many solvent scales have been developed with the aim of accurately describing solvent molecular properties but no one scale has demonstrated broad applicability.

Our approach is to combine suitable chemical properties and descriptors selected from carefully chosen solvent scales. A PCA analysis on the set of solvents and their chosen descriptors generates a set of principal components which more accurately reflect the intrinsic molecular properties of the compounds. As these principal components are typically referred to as principal properties. Our new principal properties approximately describe solvent polarity, polarisability and hydrogen bonding.



Picture 1 shows solvents grouped by family. Picture 2 shows results for a challenging SNAr reaction

Each of the new principal properties becomes a continuum. The combination of two or more principal properties provides a map which supports the rational selection of a representative subset of compounds (Carlson, R.; Carlson, J. E. *Org. Process Res. Dev.* ***2005****, 9*, 680). The use of PCA to map solvent space routinely identifies solvents which have similar principal properties but which are structurally very diverse and belong to other solvent families.

In summary PCA allows the mapping of solvents or other compounds, with a set of properties, exploring their relationships to each other and identifying underlying patterns in the data. It enables the identification of two or more principal components generating a 2D or 3D map of the solvents.

Paul Murray Catalysis Consulting provides Consulting and Training in Design of Experiments (DoE), Principal Component Analysis (PCA), homogeneous, heterogeneous and biocatalysis.

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