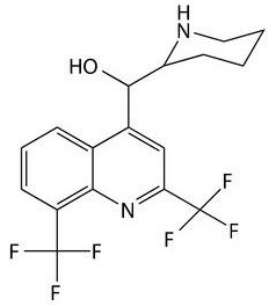
Computational Chemistry

HOW DO COMPUTERS KNOW CHEMISTRY?

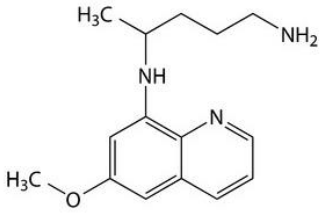
Content

- Structure and function
- Mathematics in Chemistry
- Quantitative Structure Activity Relationship (QSAR)
- Components of QSAR
- Types of QSAR
- Molecular Descriptors

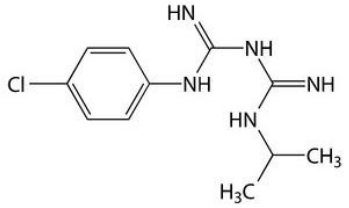
Structure and function



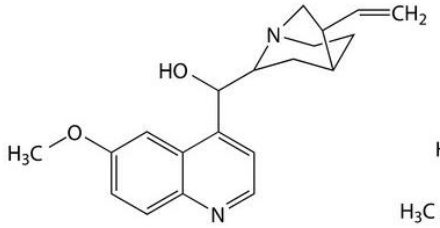
Mefloquine



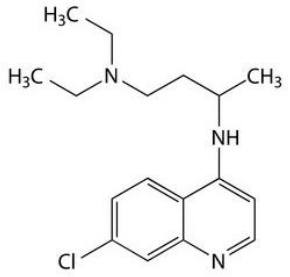
Primaquine



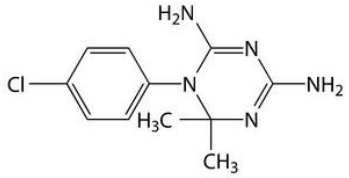
Proguanil



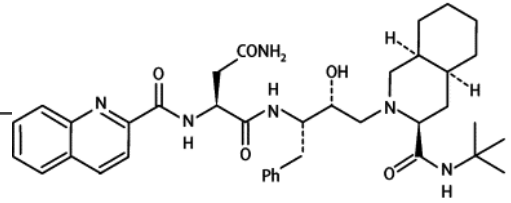
Quinine



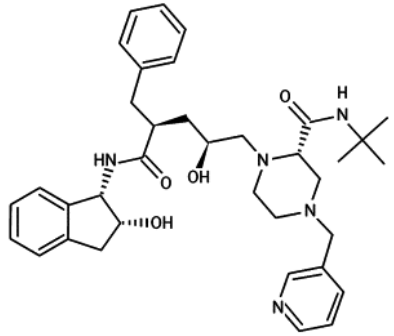
Chloroquine



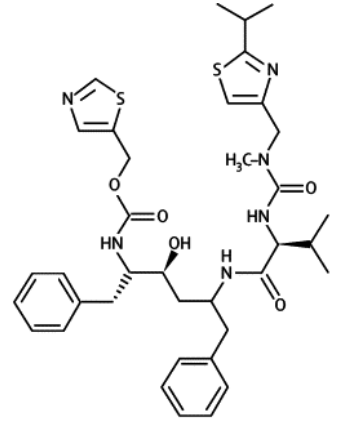
Cycloguanil



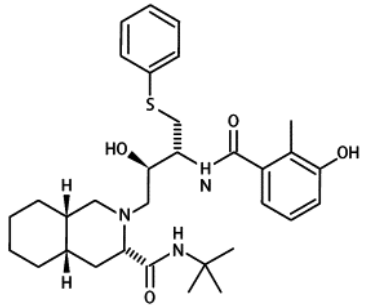
Saquinavir



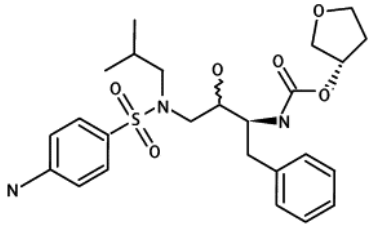
Indinavir



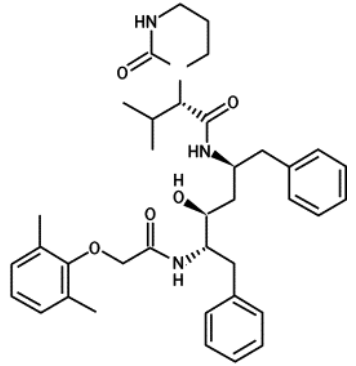
Ritonavir



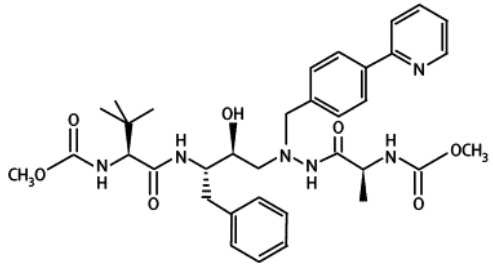
Nelfinavir



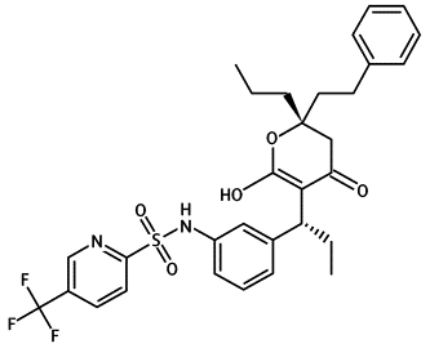
Amprenavir



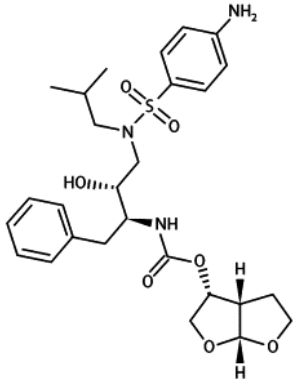
Lopinavir



Atazanavir



Tipranavir



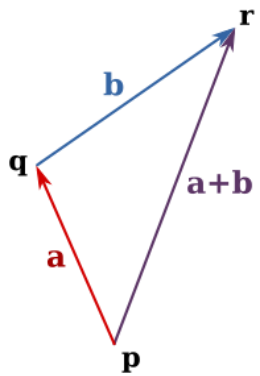
Darunavir

Mathematics in Chemistry

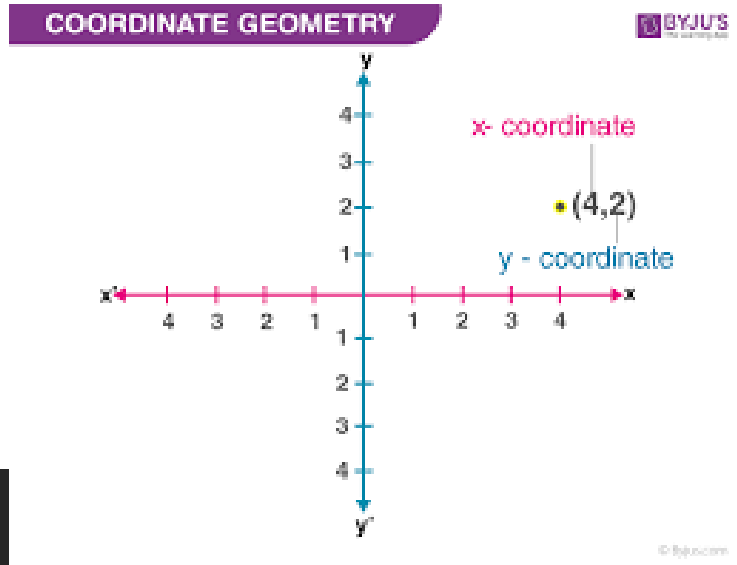
- Linear Algebra (Matrices)

$$\begin{array}{c} \\ 1 \\ 2 \\ 3 \\ \vdots \\ m \end{array} \begin{array}{c} \begin{array}{cccc} 1 & 2 & \dots & n \end{array} \\ \begin{bmatrix} a_{11} & a_{12} & \dots & a_{1n} \\ a_{21} & a_{22} & \dots & a_{2n} \\ a_{31} & a_{32} & \dots & a_{3n} \\ \vdots & \vdots & \vdots & \vdots \\ a_{m1} & a_{m2} & \dots & a_{mn} \end{bmatrix} \end{array}$$

- Vectors Algebra

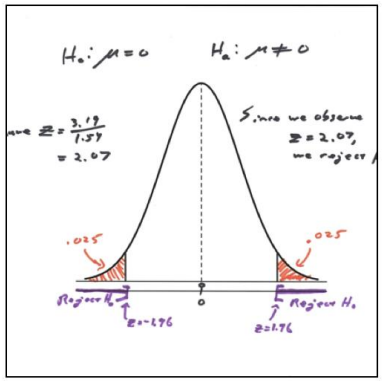


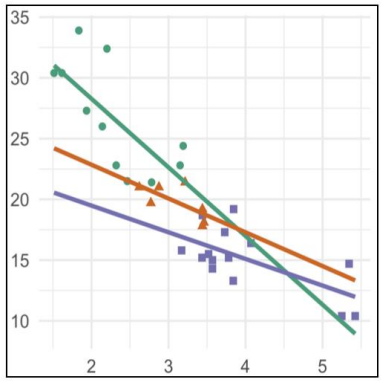
- Coordinate Geometry

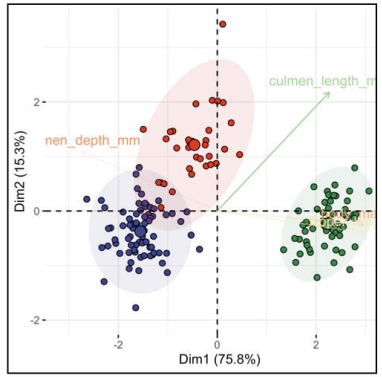


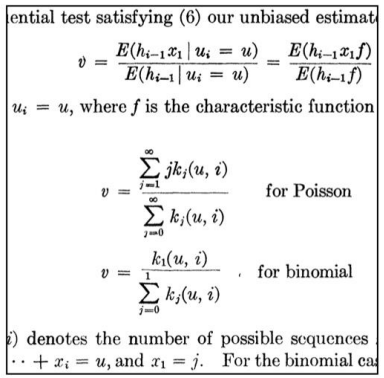
Mathematics in Chemistry

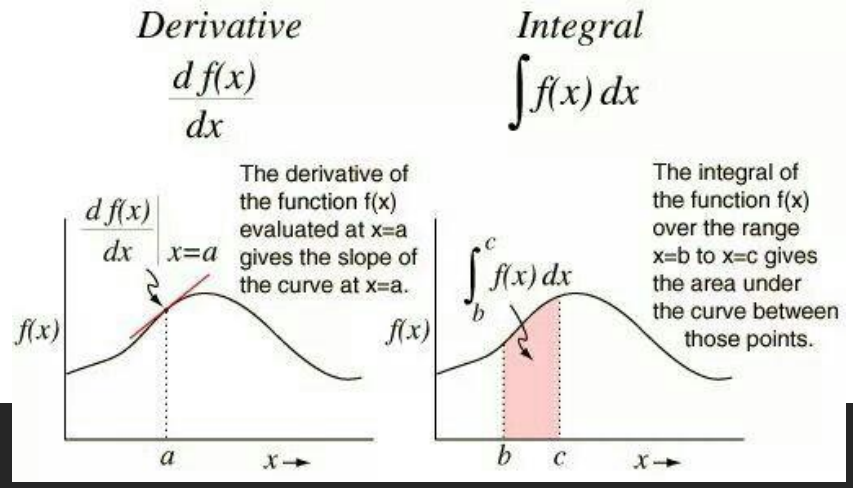
- Calculus: Derivatives and Integrations
- Statistics





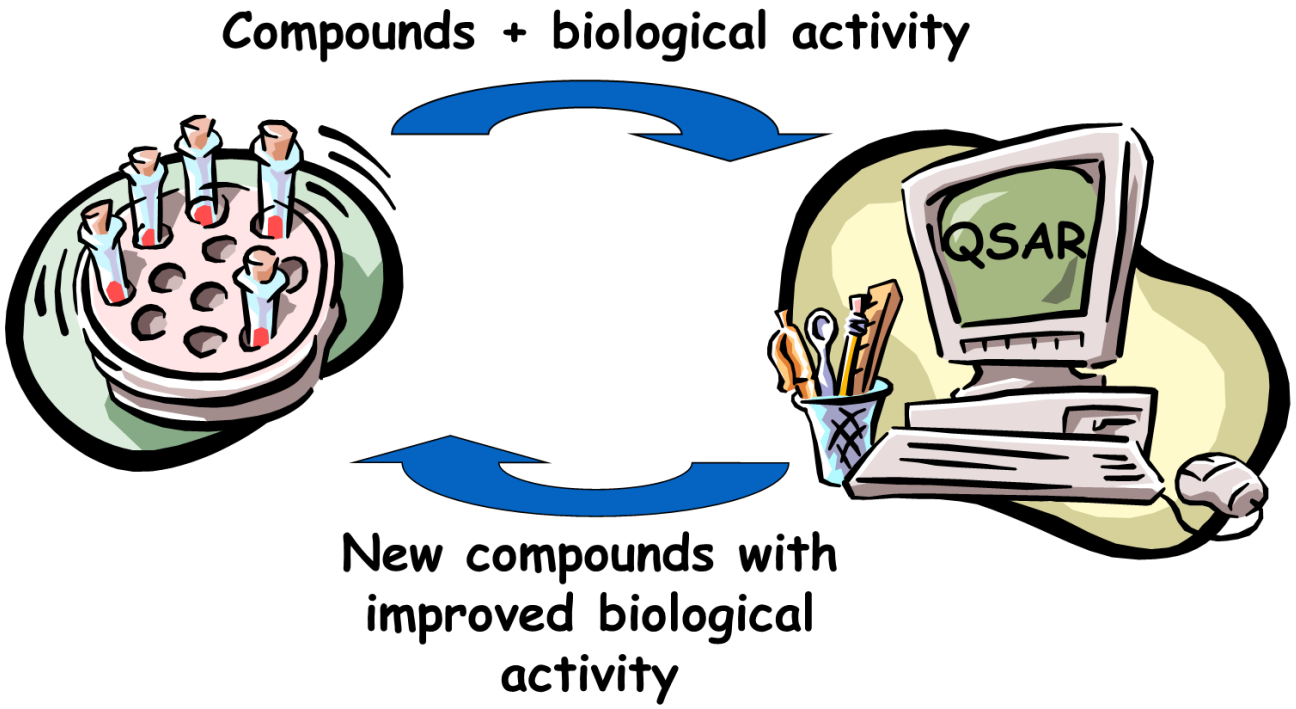




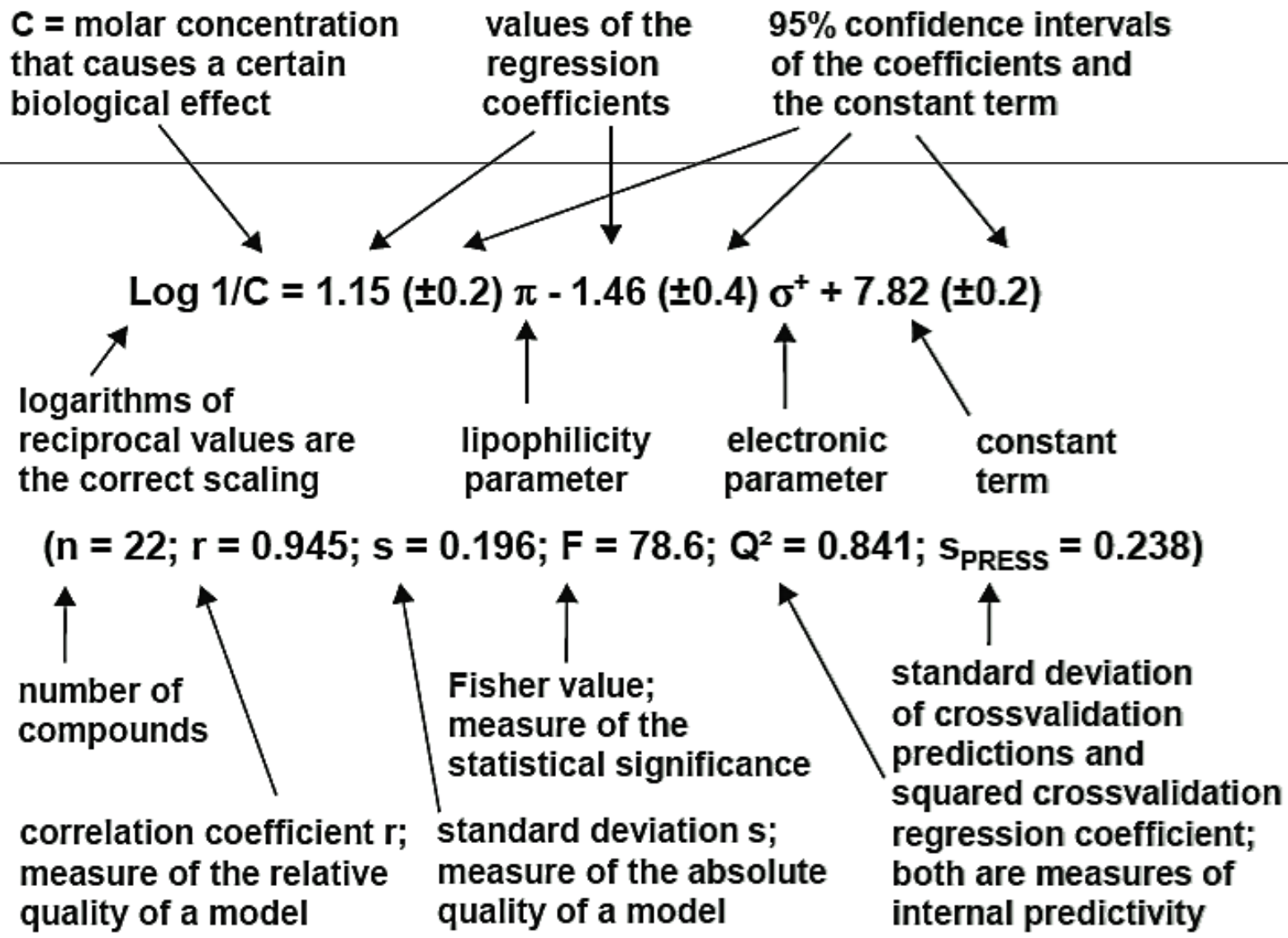


Quantitative Structure Activity Relationship

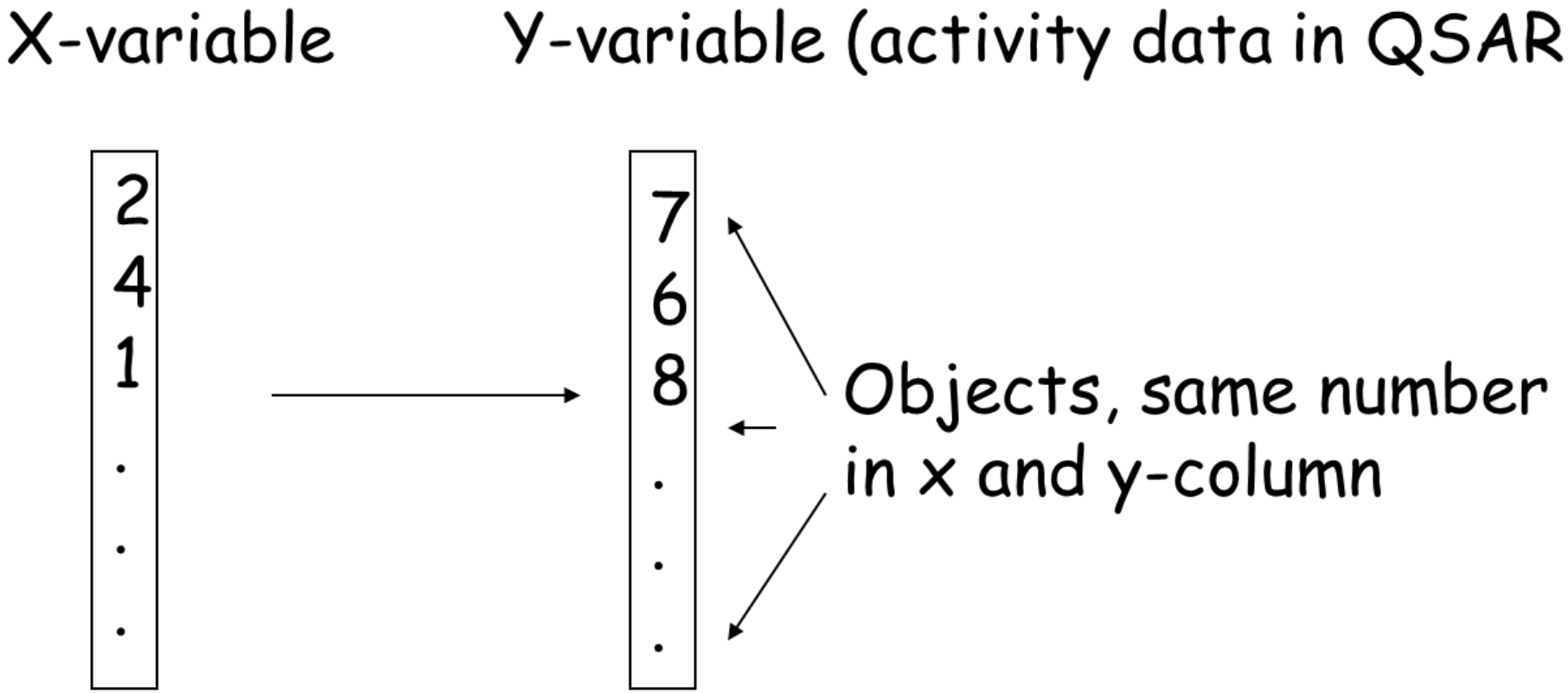
- The number of compounds required for synthesis in order to place 10 different groups in 4 positions of benzene ring is 10^4.
- Solution: synthesize a small number of compounds and from their data derive rules to predict the biological activity of other compounds



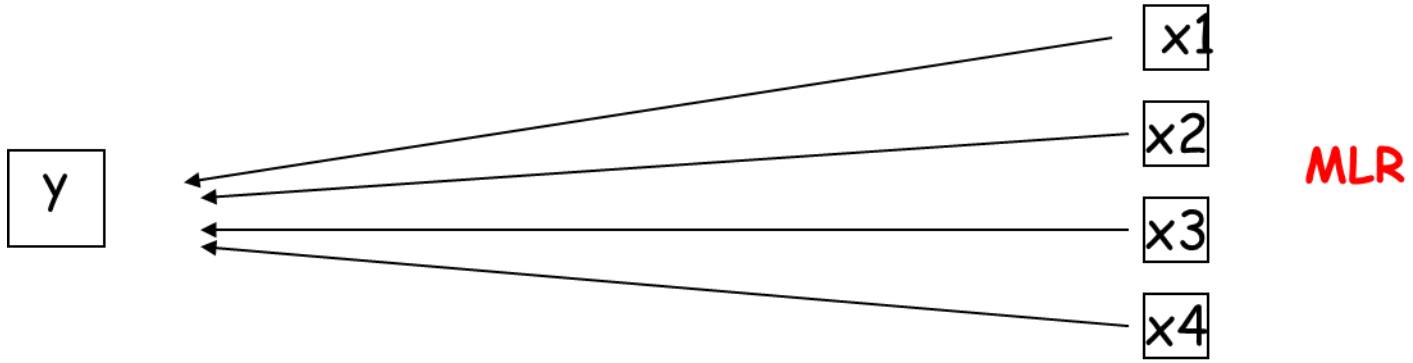
Components of QSAR



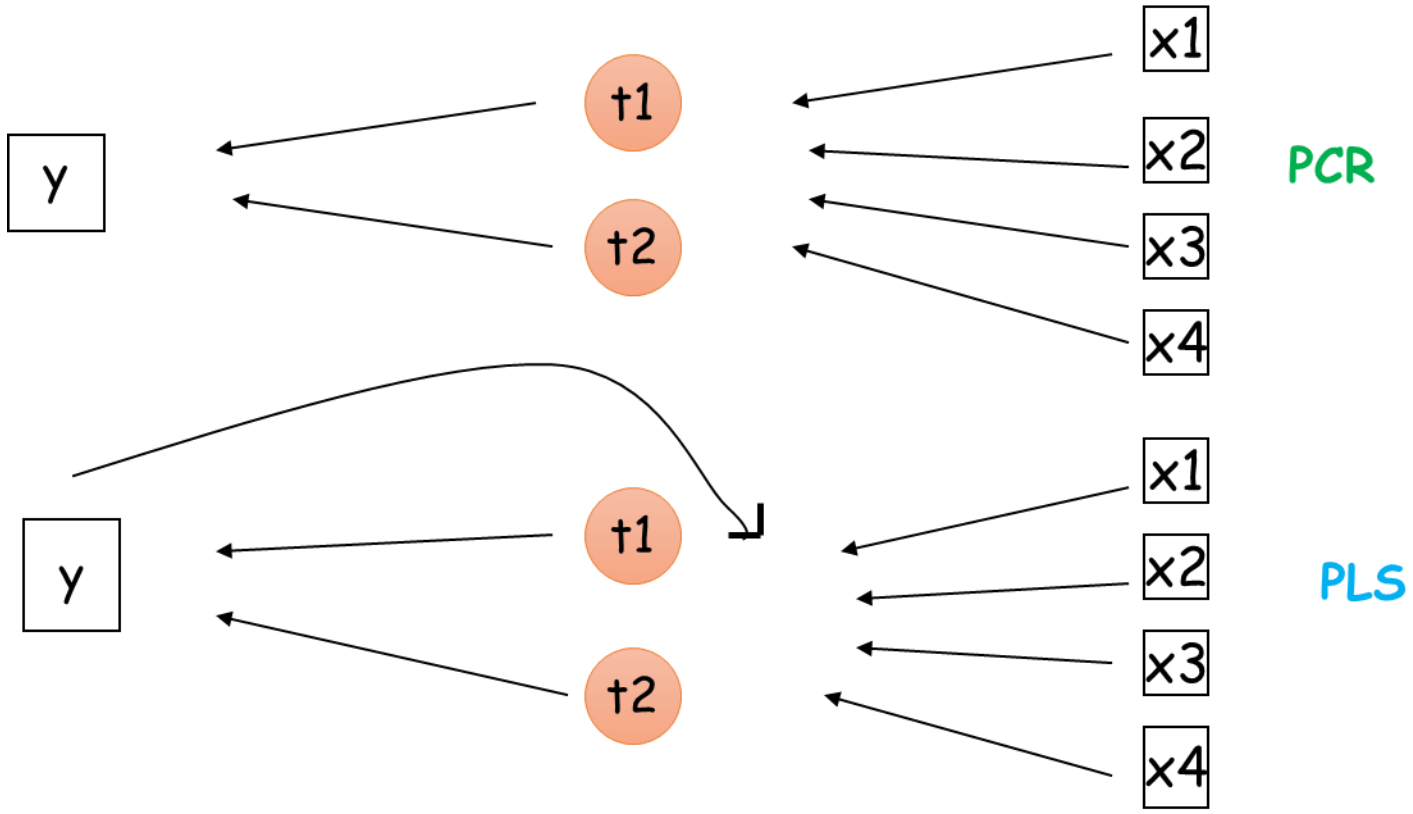
Data Structure in QSAR



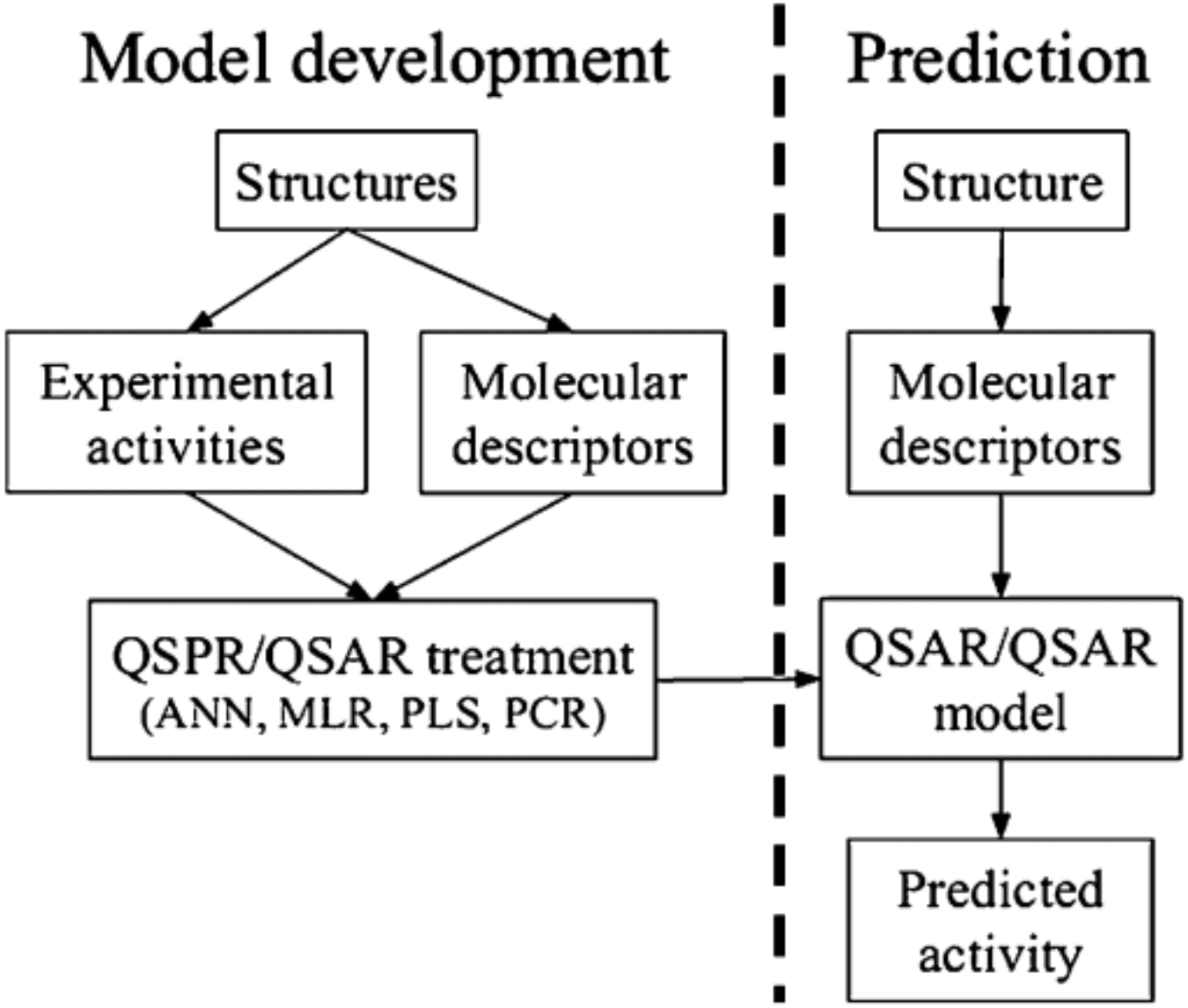
Mathematics in QSAR



Chemometrics in QSAR



Steps in QSAR



Dimensionality in QSAR

- 1D-QSAR
- 2D-QSAR
- 3D-QSAR (Receptor-dependent and Receptor-independent)
- 4D-QSAR (Receptor-dependent and Receptor-independent)
- 5D-QSAR → Induced Fit effect
- 6D-QSAR → Solvation effects

Molecular Descriptors

Molecular Property	Corresponding Interaction	Parameters
Lipophilicity	hydrophobic interactions	log P, π, f, R_M, χ
Polarizability	van-der-Waals interactions	MR, parachor, MV
Electron density	ionic bonds, dipol-dipol interactions, hydrogen bonds, charge transfer interactions	σ, *R*, *F*, κ, quantum chemical indices
Topology	steric hindrance geometric fit	E_S, r_V, L, B, distances, volumes

Type of Molecular Descriptors

- **0D-descriptors** (i.e. constitutional descriptors, count descriptors)
- **1D-descriptors** (i.e. list of structural fragments, fingerprints)
- **2D-descriptors** (i.e. graph invariants)
- **3D-descriptors** (i.e. quantum-chemical descriptors, size, steric, surface and volume)
- **4D-descriptors** (i. e. GRID or CoMFA methods, Volsurf)

What should a descriptor be like?

- Should have structural interpretation
- Should have good correlation with at least one property
- Should preferably discriminate among isomers
- Should be possible to apply to local structure
- Should possible to generalize to "higher" descriptors
- Should be simple

What should a descriptor be like?

- Should not be based on experimental properties
- Should not be trivially related to other descriptors
- Should be possible to construct efficiently
- Should use familiar structural concepts
- Should change gradually with gradual change in structures
- Should have the correct size dependence, if related to the molecule size