Kernels for kernel-based machine learning

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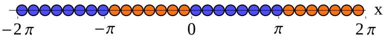
Navigating Chemical Compound Space for Materials and Bio Design
Los Angeles, California, USA, March 18, 2011

Kernels: Definition

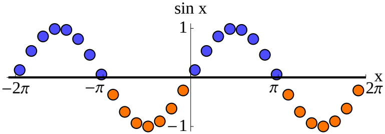
A kernel is a function that corresponds to an inner product

$$k : \mathcal{X} \times \mathcal{X} \to \mathbb{R}, \qquad k(x, z) = <\phi(x), \phi(z)> \text{ with } \phi : \mathcal{X} \to \mathcal{H}$$

Example:



$\overset{\phi}{\mapsto}$



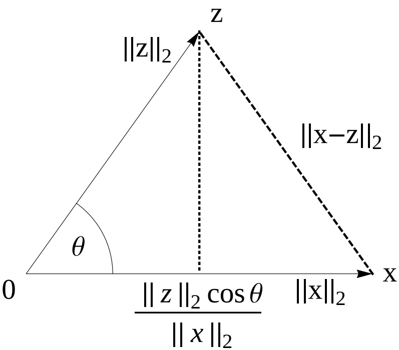
Input space

Feature space

Kernels: Geometric aspects

Kernels describe the geometry of the data

- Correspond to inner products: $k(x,z) = <\phi(x), \phi(z)>$
- Encode information about length and angle in feature space: $k(x,z) = ||\phi(x)||_2 \; ||\phi(z)||_2 \cos\theta$
- Correspond to Euclidean distance: $||\phi(x) - \phi(z)||_2^2 =$
  $$k(x,x) - 2k(x,z) + k(z,z)$$



Kernels: Characterization

A function $k : \mathcal{X} \times \mathcal{X} \to \mathbb{R}$ is a kernel if and only if
for all $n \in \mathbb{N}, x_1, \ldots, x_n \in \mathcal{X}$ the matrix $\mathbf{K} = k(x_i, x_j)$ is symmetric and

- positive semi-definite, $\forall\, \mathbf{v} \in \mathbb{R}^n : \mathbf{v}^T \mathbf{K} \mathbf{v} \geq 0$
- has only non-negative eigenvalues
- all principal minors are non-negative
- $\exists\, \mathbf{L} \in \mathbb{R}^{n \times n} : \mathbf{K} = \mathbf{L}\mathbf{L}^T \wedge \operatorname{diag}(\mathbf{L}) \geq 0$ (Cholesky decomposition)
- $f(\mathbf{v}) = \frac{1}{2}\mathbf{v}^T \mathbf{K} \mathbf{v} + \mathbf{a}^T \mathbf{v} + c$ is convex

Similar characterization for symmetric, positive definite k.

Kernel trick for distances leads to conditionally positive semi-definite kernels, where $\sum_{i=1}^{n} \mathbf{v}_i = 0$.

Kernels: Closure properties

Kernels are closed under

- Addition: $k(x,z) = k_1(x,z) + k_2(x,z)$
- Multiplication with non-negative scalar: $k(x,z) = \gamma k_1(x,z)$, $\gamma \geq 0$
- Point-wise product: $k(x,z) = k_1(x,z) \cdot k_2(x,z)$
- Tensor product $k_1 \otimes k_2$, direct sum $k_1 \oplus k_2$

Linear combination of kernels is a kernel:

$$k(x,z) = \gamma_1 k_1(x,z) + \gamma_2 k_2(x,z) + \ldots + \gamma_m k_m(x,z)$$

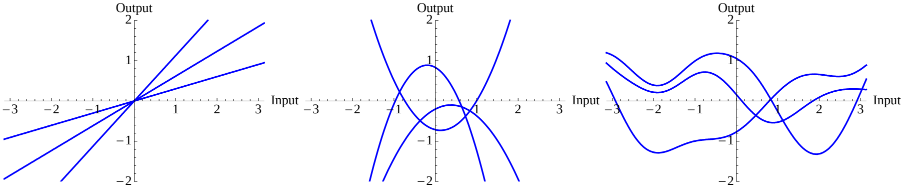
Specific kernels: Vector data

Let $\mathbf{x}, \mathbf{z} \in \mathbb{R}^d$.

- Linear kernel: $k(\mathbf{x}, \mathbf{z}) = <\mathbf{x}, \mathbf{z}>$
- Polynomial kernel: $k(\mathbf{x}, \mathbf{z}) = \left(<\mathbf{x}, \mathbf{z}> + c\right)^d$
- Squared exponential kernel (also radial basis function kernel):

$$k(\mathbf{x}, \mathbf{z}) = \exp\left(-\frac{1}{2}\frac{||\mathbf{x}-\mathbf{z}||^2}{2\sigma^2}\right)$$

Local approximator; free parameter σ (length scale)



Specific kernels: Structured data

- Convolution kernels

$$(k_1 \times \cdots \times k_d)(x, x') = \sum_{R} \prod_{i=1}^{d} k_i(x_i, x'_i)$$

- String kernels
- Kernels between probability distributions
- Kernels between graphs

Specific kernels: String kernels

Spectrum kernel

- Compare substrings of length k (k-mers)
- Position-independent
- Kernel is sum of products of counts

Example: $k = 3$

x $\boxed{\text{AAA}}$C$\boxed{\text{AAA}}$TAAGTAACTAATCTTTTAGAACTTTCAACCATTT...

z TACCTAATTATG$\boxed{\text{AAA}}$TT$\boxed{\text{AAA}}$TTTCAGCTGTGG$\boxed{\text{AAA}}$CGGAGA..

3-mer	AAA	AAC	...	TTT
# in x	2	4	...	3
# in z	3	1	...	1

$$k(x, z) = 2 \cdot 3 + 4 \cdot 1 + \ldots + 3 \cdot 1$$

Specific kernels: String kernels

Weighted degree kernel

- Compare matches at each position
- Position-dependent
- $k(x,z) = \sum_{k=1}^{d} \beta_k \sum_{i=1}^{|x|-k} \mathbf{I}\big(u_{k,l}(x) = u_{k,l}(z)\big)$

Example: $d = 3$

```
       x   AAACAAATAAGTAACTAATCTTTTAG
# 1-mers   .|.|.|||.|..||.|.|..|||.||
# 2-mers   .....||.....|.......||..|.
# 3-mers   .....|..............|.....
       z   TACCTAATTATGAAATTAAATTTCAG
```

$k(x,z) = \beta_1 \cdot 15 + \beta_2 \cdot 6 + \beta_3 \cdot 2$

Specific kernels: Graph kernels (introduction)

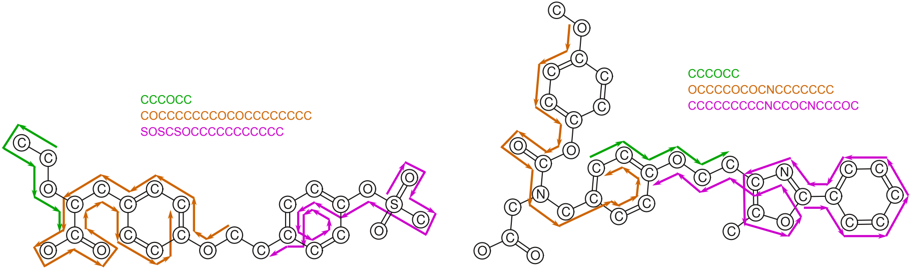
Idea: Define k directly on graphs

- Application to chemical structure graphs
- Allows direct measurement of graph similarity
- Rigorous way to combine graph theory and kernel learning

- Caveat: Complete graph kernels are computationally hard

Specific kernels: Graph kernels (overview)

- Random walk graph kernels, path-based graph kernels
- Tree pattern graph kernels, cyclic pattern graph kernels
- Graphlet kernels
- Optimal assignment graph kernels



M. Rupp, G. Schneider, Mol. Inf. 29(4): 266–273, 2010.

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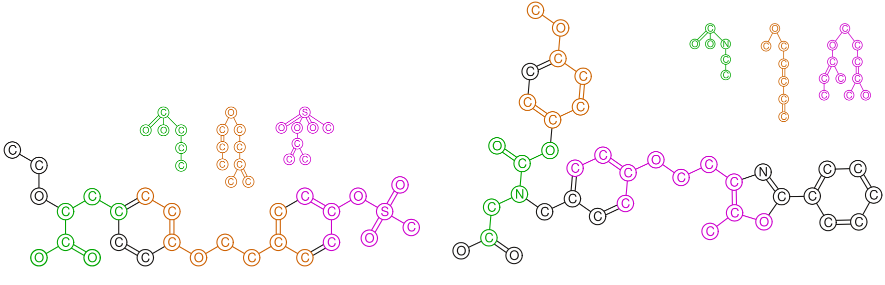

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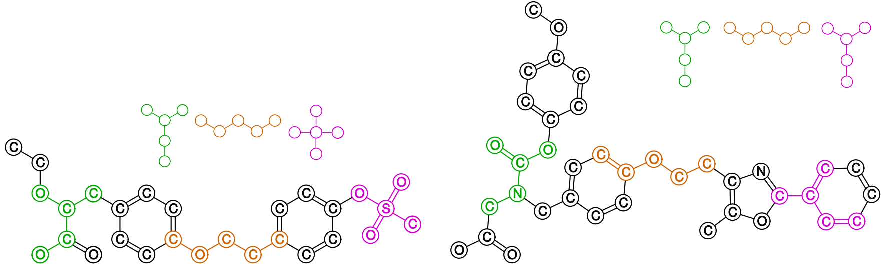

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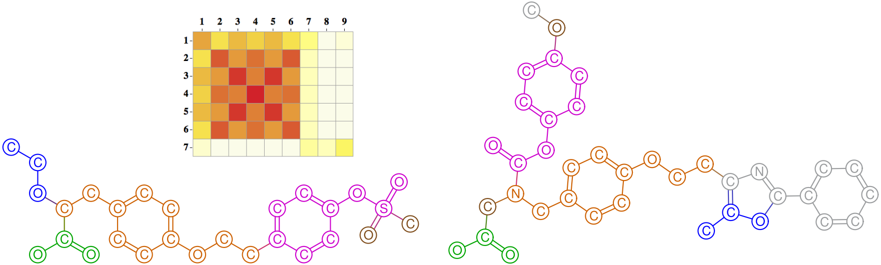

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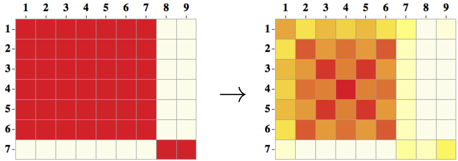
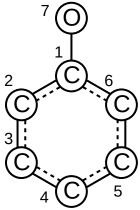
Specific kernels: Graph kernels (example)

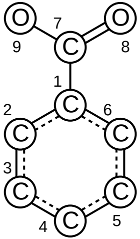
ISOAK = iterative similarity optimal assignment kernel

$$\mathbf{X}_{v,v'} = (1-\alpha)k_v(v,v') + \alpha \max_{\pi} \frac{1}{|v'|} \sum_{\{v,u\}\in E} \mathbf{X}_{u,\pi(u)} k_e\big(\{v,u\},\{v',\pi(u)\}\big)$$

α controls recursiveness; π assigns neighbors of v to neighbors of v'







Rupp et al, J. Chem. Inf. Mol. Model. 47(6): 2280, 2007.

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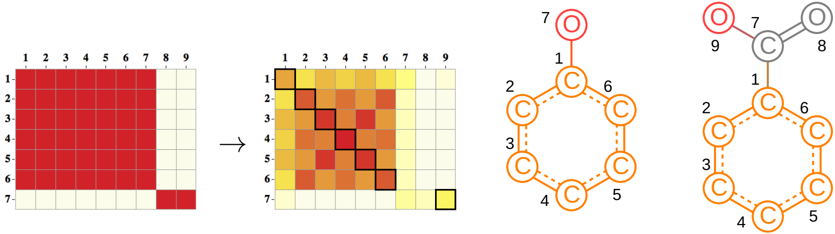
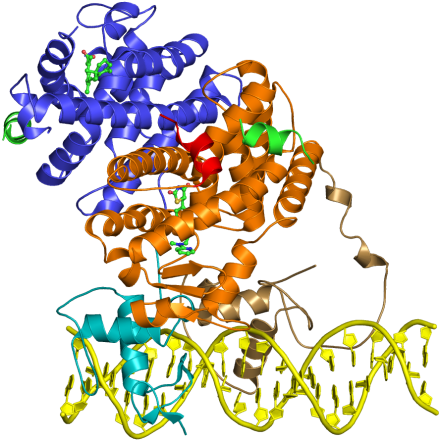


Rupp et al, J. Chem. Inf. Mol. Model. 47(6): 2280, 2007.

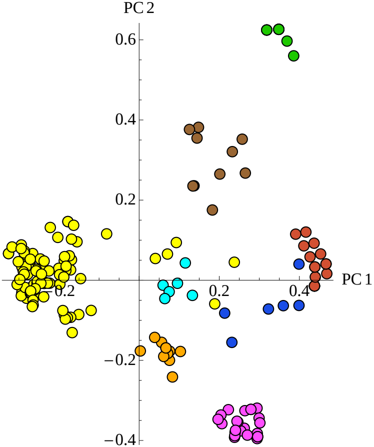
Application example: Virtual screening

Target



Peroxisome proliferator-activated receptor γ (PPARγ)

Data



Kernel principle component analysis with ISOAK graph kernel ($n = 176$)

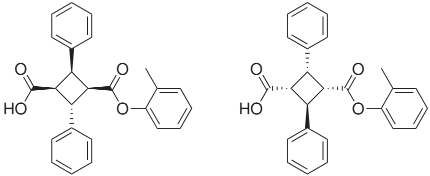
Rücker et al., *Bioorg. Med. Chem.* 14(15): 5178, 2006; Rupp, PhD thesis, 2009.

Application example: Virtual screening

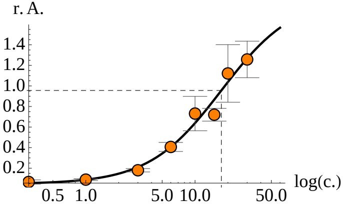
Methods:

- Graph kernel, vector kernels
- Multiple kernel learning
- Gaussian process regression

Results:



Stereochemistry



Dose-response curve

Rupp et al., *ChemMedChem* 5(2): 191, 2009

Summary

- Kernels correspond to inner products
- Well-characterized function class
- Kernels can be defined on structured data

Literature

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  110 pages, review
- M. Rupp, G. Schneider: *Graph kernels for molecular similarity*, Mol. Inf 29(4): 266–273, 2010.
  8 pages, overview of graph kernels for small structure graphs