

PhAST – Pharmacophore Alignment Search Tool

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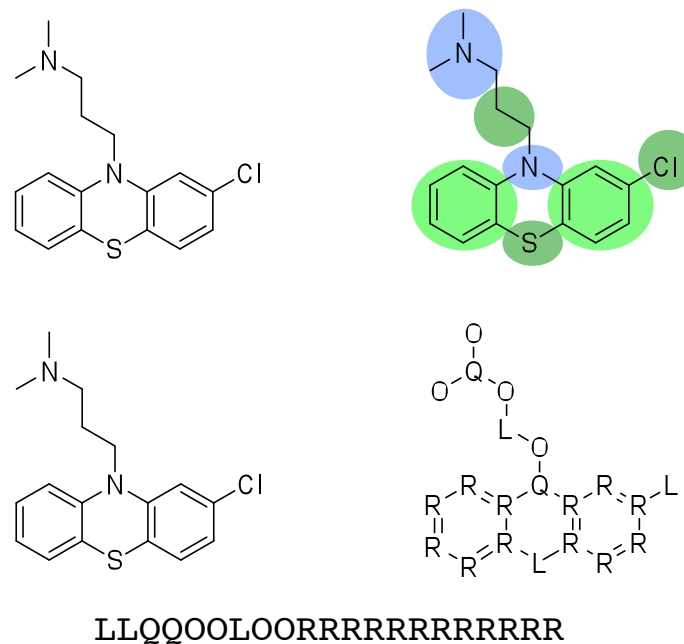
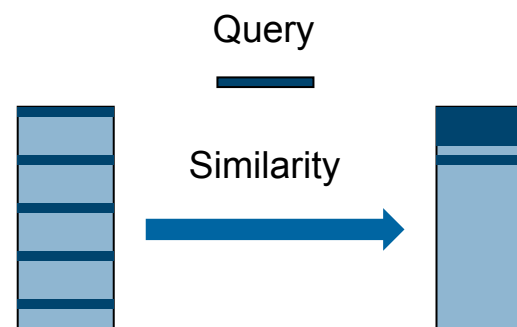
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Hähnke *et al.*, JCC 2009 / 2010



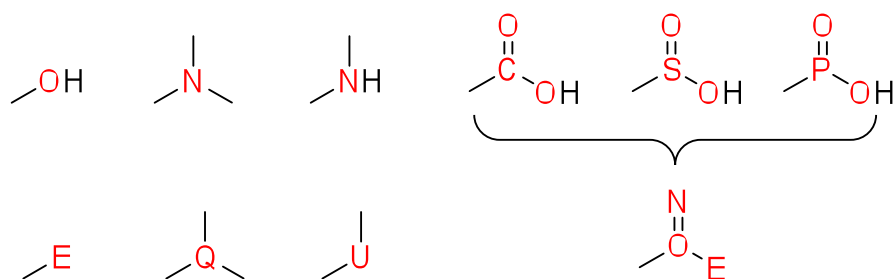
Short Facts

- Virtual Screening
- 2D Pharmacophore
- Text-based

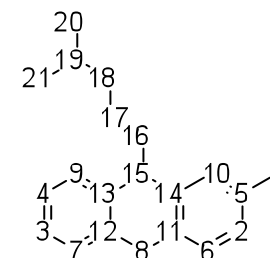
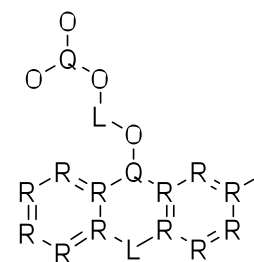
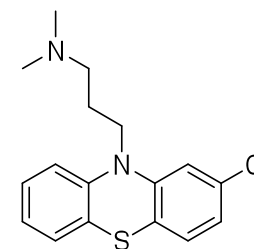


Sequence Generation

- Atomtyping
 - Fragment-based, MQL (Proschak *et al.*, 2007)
 - 19 substructures
 - 9 potential pharmacophoric points (symbols)



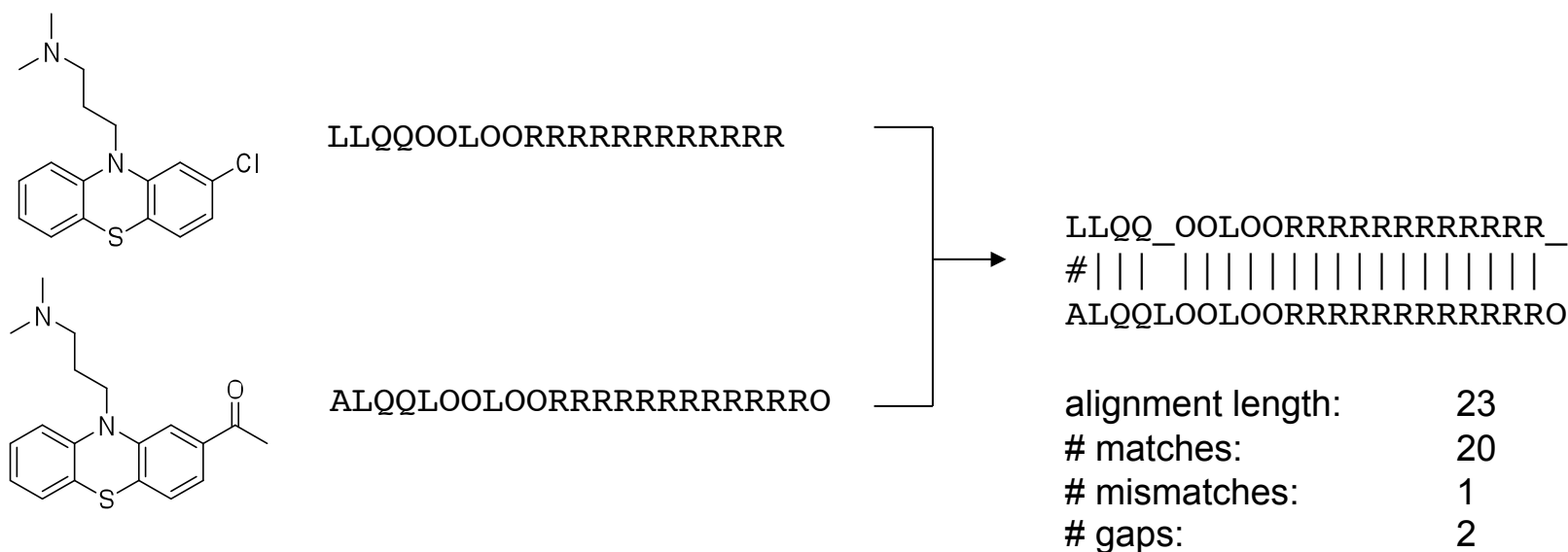
- Canonization
 - Necessary for unambiguity
 - Spectral dimensionality reduction:
Minimum Volume Embedding (Shaw & Jebara, 2007)



LRRRRRRLRRRRRRRQOLOQOO

Sequence Comparison

- Global Pairwise Sequence Alignment (Needleman & Wunsch, 1970)
 - Bioinformatics: comparison of amino acid sequences
 - Retains order of symbols
 - May insert gaps



- Similarity: alignment score

$$S = \frac{Score}{AlignmentLength}$$

Canonization & Alignment Evaluation

Performance in BEDROC scores (Truchon & Bayly, 2007)

$$PID_1 = \frac{Nomatches}{AlignmentLength}$$

$$PID_2 = \frac{actualPID_1}{\max PID_1}$$

$$S_1 = AlignmentScore$$

$$S_2 = \frac{S_1}{AlignmentLength}$$

$$S_3 = \frac{S_1}{ShortestSequenceLength}$$

	PID ₁	PID ₂	S ₁	S ₂	S ₃	Mean	StDev	CV
JG	0.255	0.166	0.351	0.356	0.352	0.296	0.084	0.284
JG m	0.244	0.151	0.346	0.352	0.346	0.288	0.089	0.308
Iso	0.281	0.188	0.389	0.389	0.384	0.326	0.090	0.276
LE	0.277	0.182	0.378	0.379	0.375	0.318	0.088	0.276
MVE d 0.4	0.291	0.199	0.397	0.400	0.397	0.337	0.090	0.267
MVE e	0.267	0.162	0.372	0.373	0.371	0.309	0.094	0.304 ∅ 0.281
PCA	0.244	0.143	0.266	0.347	0.264	0.253	0.073	0.289
Pra	0.267	0.165	0.368	0.374	0.370	0.309	0.092	0.299
Pra m	0.260	0.168	0.255	0.360	0.356	0.280	0.080	0.287
W	0.313	0.200	0.360	0.374	0.372	0.324	0.073	0.226
W m	0.290	0.168	0.362	0.371	0.369	0.312	0.087	0.280
Mean	0.272	0.172	0.350	0.370	0.360	Brenner, Chothia, Hubbard 1998:		
StDev	0.021	0.018	0.047	0.016	0.035			
CV	0.079	0.107	0.133	0.043	0.097	PID < Score < Significance		
	∅ 0.092							

time for questions