

TOPOMER COMFA

EFFORTLESS 3D QSAR



Topomer CoMFA[®] is a 3D QSAR tool that automates the creation of models for predicting the biological activity or properties of compounds. Topomer CoMFA models can be created in minutes, not days, can easily be used by both QSAR experts and QSAR non-experts, and the results are often comparable to traditional CoMFA analysis.

KEY FEATURES

EFFECTIVE

- **CADD scientists can quickly determine whether a predictive Topomer CoMFA model is possible**
- **Quantitative, predictive 3D QSAR models developed in Topomer CoMFA can be used in Topomer Search to search for and identify the substituents and R-groups that are predicted to optimize the activity of your compounds**

- **Results generally comparable to traditional CoMFA analysis**

FAST

- **Results typically obtained in minutes, not days**

EASY

- **Automates the time consuming task of aligning structures prior to 3D-QSAR analysis**
- **Very usable by both the occasional QSAR user and the CoMFA expert**

Lead optimization and the value of 3D QSAR

Wouldn't you like to have the ability to predict which structural changes will optimize the biological properties of your lead series? Wouldn't it be nice if you could quickly identify and suggest new R-Groups that are predicted to optimize biological properties? With Topomer CoMFA, the power of quantitative 3D-QSAR activity predictions can be harnessed to solve these problems.

Classical 3D QSAR methods, such as Comparative Molecular Field Analysis (CoMFA[®]), often provide accurate prediction of biological activity. CoMFA models are very interpretable and suggestive of chemical changes that will improve biological activity. However, these methods can require time-consuming, expert preparation (molecular alignment, conformer selection). Topomer CoMFA minimizes the preparation needed for 3D QSAR analysis through an entirely objective and consistent set of alignment rules. This means that a predictive 3D QSAR model can be produced in minutes by experts and non-experts alike.

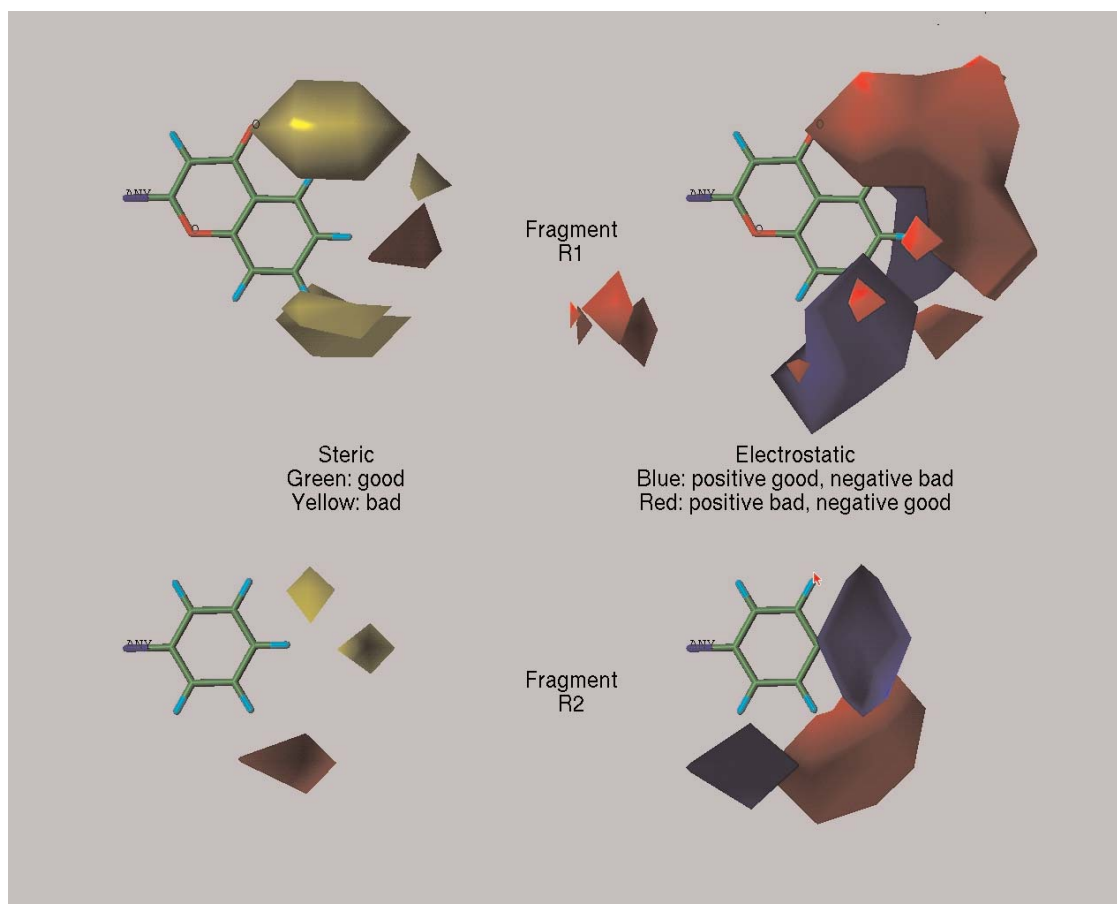
Topomer CoMFA results are often comparable to results obtained from laborious manual alignment and analysis. Fifteen (15) 3D QSAR analyses taken from the literature, consisting of 847 structures, were remodeled successfully using Topomer CoMFA (average q^2 of 0.520 compared with the literature average q^2 of 0.636). The average standard deviation of prediction for 133 compounds of 0.688, compared with the optimized literature alignments giving 0.553 or 0.75 kcal/mole, shows that the Topomer CoMFA models, built in minutes, can be applied predictively and with excellent accuracy compared to other methods. These studies have recently been extended to an additional six (6) datasets with comparable results. (G. Stahl, RD Cramer, B. Wendt (2007). Topomer CoMFA: Investigation of scope. Presented: 234th American Chemical Society National Meeting, Boston, MA Aug 19-23). Conformer selection and alignment with Topomer CoMFA is entirely objective and automated, allowing Topomer CoMFA models to be used for virtual screening by Topomer Search. You can use your compound collection as a source of structural fragments and to identify R-groups or substituents that would be predicted by the 3D QSAR model to optimize the biological properties of your series. This is something you just can't do with traditional 3D QSAR models based on manual alignments.

HARDWARE AND SOFTWARE REQUIREMENTS

Software: Topomer CoMFA is available through the SYBYL graphical interface and requires a separate license in addition to SYBYL Base. A license for CONCORD is also required to run Topomer CoMFA.

Hardware: Topomer CoMFA and SYBYL run on IRIX® (SGI®) and Linux® (x86).

Topomer CoMFA automates the creation of models for predicting the biological activity or properties of compounds. Topomer CoMFA models can be created in minutes, not days, can easily be used by both QSAR experts and QSAR non-experts, and the results are often comparable to traditional CoMFA analysis. Use Topomer CoMFA in concert with Topomer Search to identify the substituents and R-groups that are predicted to optimize the activity of your compounds using Topomer CoMFA's quantitative, predictive 3D QSAR models.



Topomer CoMFA contour plots explain how changes in the steric and electrostatic properties of your compounds can be modified to improve biological properties. These plots suggest regions where increasing steric bulk either enhances or diminishes activity, or regions where positive (or negative) electrostatic groups are predicted to improve activity.

COMPLEMENTARY SOFTWARE

QSAR with CoMFA®	Concord® (required)
HQSAR™	Almond™
Topomer Search	

REFERENCES & FURTHER READING

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WWW.TRIPOS.COM			CONTACT_US@TRIPOS.COM	
FRANCE +33 1 69 59 29 49	GERMANY +49 89 45 10 300	JAPAN +81 3 3662-0521	AUSTRALIA +61 (7) 5439 9775	UNITED STATES 800-323-2960 +1-314-647-1099
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