

第 51 回熱測定ワークショップ
第 5 回生体分子間相互作用解析フォーラム研究会

Workshop on the Analysis of ITC Data

会 期:2014 年 6 月 28 日(土)

会 場:大阪大学医学工学研究科 東京ブランチ 東京都中央区日本橋本石町 4-4-20

主 催:日本熱測定学会、生体分子相互作用解析フォーラム

使用言語:英語(必要に応じた日本語での説明)

参加費:5,000 円(終日参加を前提とします)

注意事項:ご参加にはノート型パソコンのご持参をお願いします。

(Microsoft® Windows®がインストール済のもの(バージョンは問いません))

プログラムのインストール、デモデータのダウンロード等の詳細はお申し込み頂いた方に、別途、ご連絡いたします。

企画世話人:内山 進(大阪大学)、有坂文雄(東京工業大学)、織田昌幸(京都府立大学)、
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ワークショップ概要

等温滴定型熱量計(ITC)による分子間相互作用解析は、創薬等において有用な手法で、とくに微量で測定可能な装置が登場してから盛んに利用される状況になってきました。今回、ITCデータの解析用プログラム SEDPHAT を開発した NIH(米国立衛生研究所)の Zhao 博士、テキサス大学の Brautigam 博士ら複数の研究者を招き、SEDPHAT を用いた ITC データの解析法に関するワークショップを開催いたします。複数データの同時解析や、より複雑なモデルを用いた解析を行いたい方、さらには ITC による解析に疑問をお持ちの方は、是非、この機会をご利用いただければと思います。

参加申込方法: 参加をご希望の方は、以下の申込先まで、氏名および所属をメールにてご連絡ください。なお、熱測定学会の会員の方は、その旨をあわせてご記載下さい。

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Instructors: Chad Brautigam (The University of Texas Southwestern Medical Center, Dallas, TX, USA) and Huaying Zhao (National Institutes of Health, Bethesda, MD, USA)

Program

1000 – 1100 Lecture: NITPIC, SEDPHAT, and GUSI: Novel approaches to the integration, analysis, and presentation of ITC data.

- Brief intro to ITC and standard integration/analysis/presentation
- NITPIC
 - Estimation of injection endpoint
 - Baseline calculation
 - Parameter adjustment
 - Noise estimate (error bars)
 - End result: less noisy, less biased isotherms with error estimates
- SEDPHAT
 - Incompetent fractions or concentration error parameters, not N, are essential for global analysis
 - Treatment of thermodynamics, mass action
 - Statistically weighted fitting
 - Global capabilities, many models
- GUSI
 - Quick, parses data automatically, has new data-presentation formats
 - Produces publication-quality plots

1100 – 1115 BREAK

1115 – 1130 Lecture: Organization principles for NITPIC, SEDPHAT, and GUSI.

- NITPIC
 - Input: .itc files (no transformation needed) or .xml files from NanoAnalyze
 - Organization; view window vs. Control Panel
 - Execution and Exporting
 - Show all files exported by NITPIC
 - Restarting; the .nitpkl file; portability
- SEDPHAT
 - Loading the .sedphat file—what else gets loaded?
 - Model Choices
 - Global vs. Local Parameters
 - Run vs. Fit
 - Saving options—local vs. path-independent
 - Documenting Results
- GUSI
 - Should work seamlessly with SEDPHAT
 - Same window organization as NITPIC
 - Saving formats
 - Figures
 - States—a state is completely self-contained and portable

1130 – 1200 Practical: Basic ITC Analysis with NITPIC, SEDPHAT, and GUSSI

- NITPIC
 - Loading files
 - Execution
 - Examination of results; zoomed injection graphs
 - Legend and Save tabs
 - Export Everything
- SEDPHAT
 - Started from NITPIC
 - Double-check Exp. Parameters (weighted fitting activated!), verify Global Parameters
 - Run, Fit
 - Saving results
 - Send plot to GUSSI
- GUSSI
 - Should start from SEDPHAT
 - Maximize/Minimize Control Panel frames
 - Elementary changes; colors, lines, error bars, residuals
 - Saving data, figures, states

1200 – 1300 LUNCH

1300 – 1400 Practical: Advanced Analyses

- NITPIC
 - Detailed descriptions of Control Panel items
 - Examples of what to do if:
 - Too much injection included
 - Too little injection included
 - Too many shape components included
 - Buffer subtraction
 - Serial Execution
- SEDPHAT
 - Exclusion of data points
 - Parameter restraints
 - Buffer subtraction
 - Constraints of parameters
- GUSSI
 - Multiple thermogram/isotherm pairs; legends
 - Turning on/off thermograms and residuals
 - Axis limits; custom text
 - Capturing and changing startup preferences

1400 – 1430 Lecture: Global Modeling of ITC Data

- Concepts of global analysis
- Global vs. local parameters; incompetent fractions vs. concentration errors
- Examples of multi-site models, cooperativity
- First touch of GMMA?

- Heat Capacity
 - Experiments performed at different temperatures
 - Correlation with buried surface area
 - Linkage binding models (protonation, salt)
- 1430 – 1500 Practical: Global Modeling of ITC Data**
- Mechanics of loading multiple data sets
 - Two-site binding
 - Competitive binding
 - Cooperative binding, three-site
 - Proton linkage
 - Salt linkage
 - Data simulation
- 1500 – 1515 BREAK**
- 1515 – 1545 Lecture: Statistical Concepts in SEDPHAT**
- What is the goodness-of-fit statistic in SEDPHAT?
 - What is the reduced χ^2 statistic?
 - Differential weighting of experiments
 - Fisher Statistics and ratios of χ^2 .
 - The covariance matrix vs. error-surface projection
 - Optimization Algorithms
 - Simplex
 - Marquardt-Levenberg
- 1545 – 1615 Practical: Statistical Analysis in SEDPHAT**
- Monte-Carlo simulation of errors
 - Confidence intervals by error-surface projection
 - 1-d and 2-d error-surface plotting
- 1615 – 1700 Lecture and Practical: GMMA**
- Concept of global multi-method analysis (GMMA)
 - Probing the interactions with different observables to obtain better understanding
 - Different data sets offer mutual constraints to each other in global analysis
 - Improved resolution and precision of the thermodynamic parameters
 - Brief introduction on synergies of ITC, AUC, SPR biosensing and spectroscopic methods
 - GMMA application on a 1:2 binding system
 - Advanced statistical tools in SEDPHAT for GMMA