



# SiriusT3

Fully automated titrator  
UV/VIS platform for drug  
characterization and  
compound screening



## Highly accurate $pK_a$ , Log P/D and solubility measurements

The SiriusT3™ system is a fully automated solution for drug characterization. Integrating seamlessly with analytical workflows in drug discovery, it helps researchers to identify the most promising drug candidates rapidly and efficiently, reducing the risk of late-stage failures. An integral tool for compound screening, the SiriusT3 system enables highly accurate  $pK_a$ , Log P/D and solubility measurements in a single instrument using sub-mg of sample.



**Comprehensive Data,  
Confident Decisions**



**$pK_a$  Perfection**



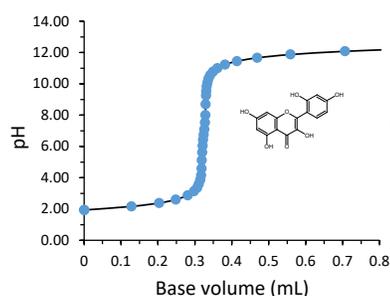
**Advanced Automation**

Determine  $pK_a$  values using two techniques: spectrometric (for UV-active compounds) (Fig. 1) and potentiometric (for both UV and non-UV active compounds). With high throughput automated screening capabilities, SiriusT3 system can complete up to 80 assays a day.

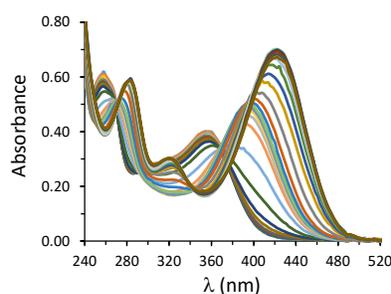
Unlike traditional shake flask methods, the SiriusT3 system provides comprehensive detailed information about the behavior of pharmaceutical drugs from titration curves, UV data, and time dependent solubility.

Pion's unique, proprietary Cheqsol method enhances instrument capabilities enabling the accurate determination of kinetic and intrinsic solubilities for ionizable compounds, characterization of supersaturation behavior and the generation of pH-solubility profiles. The SiriusT3 system is the only commercially available fully automated system combining *in vitro* physicochemical property measurements with high-throughput screening capabilities.

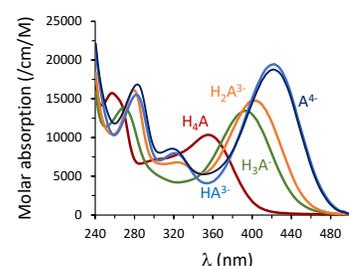
**Figure 1. Spectrometric  $pK_a$  Determination**



To determine the  $pK_a$ s of the ionizable groups of Morin, the SiriusT3 system performs a titration from pH 2-12.



At each point of the titration curve, a full UV-VIS spectrum is collected. The different spectral shapes result from the changes in Morin's ionization state.



The SiriusT3 software deconvolutes the spectra to provide the underlying spectrum of each individual species and to determine the  $pK_a$  of each ionizable group.

## The Pion Advantage



### Comprehensive Data, Confident Decisions

With online monitoring, the SiriusT3 system provides detailed titration curves and UV/VIS spectra collected at every single pH to help researchers to make quick decisions.



### $pK_a$ Perfection

High throughput  $pK_a$  screening; fully automated assays producing results in ~6 mins per titration. Validated  $pK_a$  data by applying both spectroscopic and potentiometric techniques.



### Advanced Automation

Generating detailed information about the extent and duration of compounds' supersaturated states, intrinsic and kinetic solubilities, and pH-solubility within a single automated assay in less than two hours.

# Product Configurations

SiriusT3 Configurations (number of dispensers)		
	Fully Automated	Single Vial
Spectroscopic + Potentiometric	<b>SiriusT3 DTAu (6)</b>  Fully automated system including the dispenser module, titrator module, spectrometer, and autoloader. Suited for both potentiometric and spectroscopic use with 192 automated vial positions.	<b>SiriusT3 DTu (5)</b>  A 'one vial' system consisting of a dispenser module, titrator module and spectrometer. This system has both potentiometric and spectroscopic assay capabilities.
Potentiometric only	<b>SiriusT3 DTA (5)</b>  A fully automated system including the dispenser module, titrator module and autoloader with no spectrometer. This system has potentiometric assay capability with use of 192 automated vial positions.	<b>SiriusT3 Lite (3)</b>  A 'one vial' system consisting of a dispenser module and titrator module only. This system does not contain the spectrometer and autoloader, therefore allows automated potentiometric assay capabilities.

## Software

Our software integrates **SiriusT3 Control** which allows the full automation of the system, and **SiriusT3 Refine** for the data processing, applying complex computational algorithms to produce high integrity data.

An optional upgrade of the software is **Assay Expert**, an integrated prediction module for structural analysis and the identification of ionizable groups. Determine acidity/basicity and estimate  $pK_a$  and  $\log P$  values. Use the resulting data to optimize experimental design. (Fig. 2)

The screenshot displays the Assay Expert software interface. On the left, the 'Import Molecule Data' window shows the chemical structure of piroxicam with three ionizable groups highlighted: a carboxylic acid group (pKa 4.50 (A)), a secondary amine group (pKa 13.33 (A)), and a tertiary amine group (pKa 3.54 (B)). Below the structure is a table of properties:

Property	Value
<input checked="" type="checkbox"/> pKa 1	3.540 (base)
<input checked="" type="checkbox"/> pKa 2	4.500 (acid)
<input type="checkbox"/> pKa 3	13.330 (acid)
<input type="checkbox"/> Neutral logP	1.71
<input checked="" type="checkbox"/> Intrinsic solubility	806 $\mu$ M
<input checked="" type="checkbox"/> Molecular weight	331.35
<input checked="" type="checkbox"/> Formula weight	331.35

In the center, the 'Samples' window shows the configuration for 'piroxicam':

- Sample name: piroxicam
- Sample by: Volume
- Sample volume: 5.00  $\mu$ L
- Solvent: DMSO
- Sample concentration: 10.000 mM
- Solubility: 806  $\mu$ M
- Formula weight: 331.35 g/mol
- Molecular weight: 331.35
- Number of pKas: 2
- Sample is a: Ampholyte
- Individual pKa ionic env...: No
- Ionic strength: 0.150 M
- Temperature: 25.0°C
- Base pKa 1: 3.54 (Type: Base)
- Acid pKa 2: 4.50 (Type: Acid)
- logP (XH2 +): -10.00
- logP (neutral XH): 1.71
- logP (X -): -10.00

On the right, the 'Standard Experiment Settings' window shows titration parameters:

- Category: pKa, Type: Fast UV pKa
- General Settings: Analyst name
- Standard Experiment Settings: Number of titrations (3), Minimum pH (2.000), Maximum pH (12.000)
- Assay Medium: Cosolvent in use (No), ISA water volume (1.50 mL)
- Buffer: Buffer type (Neutral Linear Buffer), Volume of buffer introduced (0.025000 mL), Buffer added (Automatic)
- Titration 1: Titrate from (Low to high pH)
- Titration 2: Titrate from (Low to high pH), Add additional water (0.00 mL)
- Titration 3: Titrate from (Low to high pH), Add additional water (0.00 mL)

Figure 2. **Assay Expert** helps to design the optimal experiment using prediction methods licensed from ACD/Labs.

## Dimensions and Weight

SiriusT3		
Model	Dimensions (H × W × D)	Weight
DTAu	700 × 825 × 460 mm	85 kg
DTu	700 × 475 × 460 mm	58 kg
DTA	700 × 825 × 460 mm	85 kg
LITE	700 × 475 × 460 mm	58 kg



## Technical Specifications

<b>pH range:</b>	1.8 - 12.2, standardization by Sirius Four-Plus
<b>pH electrodes:</b>	Contain Ag/AgCl, double junction reference
<b>Stirrer:</b>	Computer-controlled overhead with variable speed
<b>Temperature control:</b>	Peltier, range 12°C to 70°C
<b>Reagents:</b>	Water, acid, base, partition solvent and cosolvent
<b>Partition solvents:</b>	Supports 7 different ones, including Octanol, Dodecane, and Toluene
<b>Cosolvents:</b>	Supports 10 different ones, including methanol, acetonitrile, DMSO, and MDM
<b>Precision dispensers:</b>	0.5 mL, and 2.5 mL syringes with a multi-tip capillary bundle
<b>Fully automated probe:</b>	X-Y axis movement on titrator module
<b>Wash station:</b>	Provides static and flowing washes
<b>Autoloader:</b>	Holds up to 192 samples, automatic gripper arm for transfer to sample position
<b>Purge gas:</b>	Two internal flow meters, nitrogen or argon supply required
<b>Assay volumes:</b>	From 1.0 to 3.2 mL
<b>Pass-through light detection to monitor turbidity – percentage light detected reported to 0.1%</b>	

## Why Use Pion

Pion scientists are proud to be the world's leading experts in the determination of physicochemical properties. We developed the SiriusT3 instrument to characterize physchem parameters such as  $pK_a$  and log P/D and are recognized as setting the industry standard. We know that accurate determination is essential to select the right candidates in order to define the optimal path for drug development.

Pion empowers the pharmaceutical R&D community helping to make important decisions on candidate selection based on trusted data for drug optimization, which will impact people's lives. In other words, we help scientists to find the right answers faster to select the best strategy for a successful drug.

### PION ANALYTICAL SERVICES

**Don't have the time or equipment to do your own assays? Send them to us!**

Pion Analytical Services offers comprehensive  $pK_a$ , Log P/D and solubility assays on our SiriusT3 platform.