

A Proposal of New Workflow for the LC & SFC Preparation/Purification

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***HPLC 2019 Kyoto
Kyoto University, Kyoto Japan***

Welcome to Kyoto, A Home to Shimadzu!!

- 794 Kyoto became the Japan's capital city
- 1868 Tokyo became the new Japan's capital city
(ending Edo-era and starting Meiji-era)



Capital

京 都

Kyo to

Capital

Eastern

Capital

東 京

To kyo

Welcome to Kyoto, A Home to Shimadzu!!



History

1875	Genzo Shimadzu Sr. started the manufacture of educational physical and chemistry instruments in Kiyamachi-Nijo, Kyoto.
1877	Succeeded in Japan's first manned balloon flight.
1896	Succeeded in taking radiographs.
1897	Started the manufacture of storage batteries.
1909	Built Japan's first medical X-ray device.
1915	Started manufacture of optical measuring instruments.
1917	Reorganized Shimadzu as joint-stock company, with storage battery department established as separate company.
1920	Established Dalian office.
1930	Genzo Shimadzu Jr. was invited to the Emperor's dinner party as one of the ten greatest inventors of Japan.
1933	Developed industrial X-ray device.
1934	Developed Japan's first spectrograph.



Genzo
Shimadzu



Genzo
Shimadzu Jr.

Contents

1. Introduction

2. Analytical SFC

3. Semi-Preparative SFC

4. Preparative LC



1) Introduction

41 years

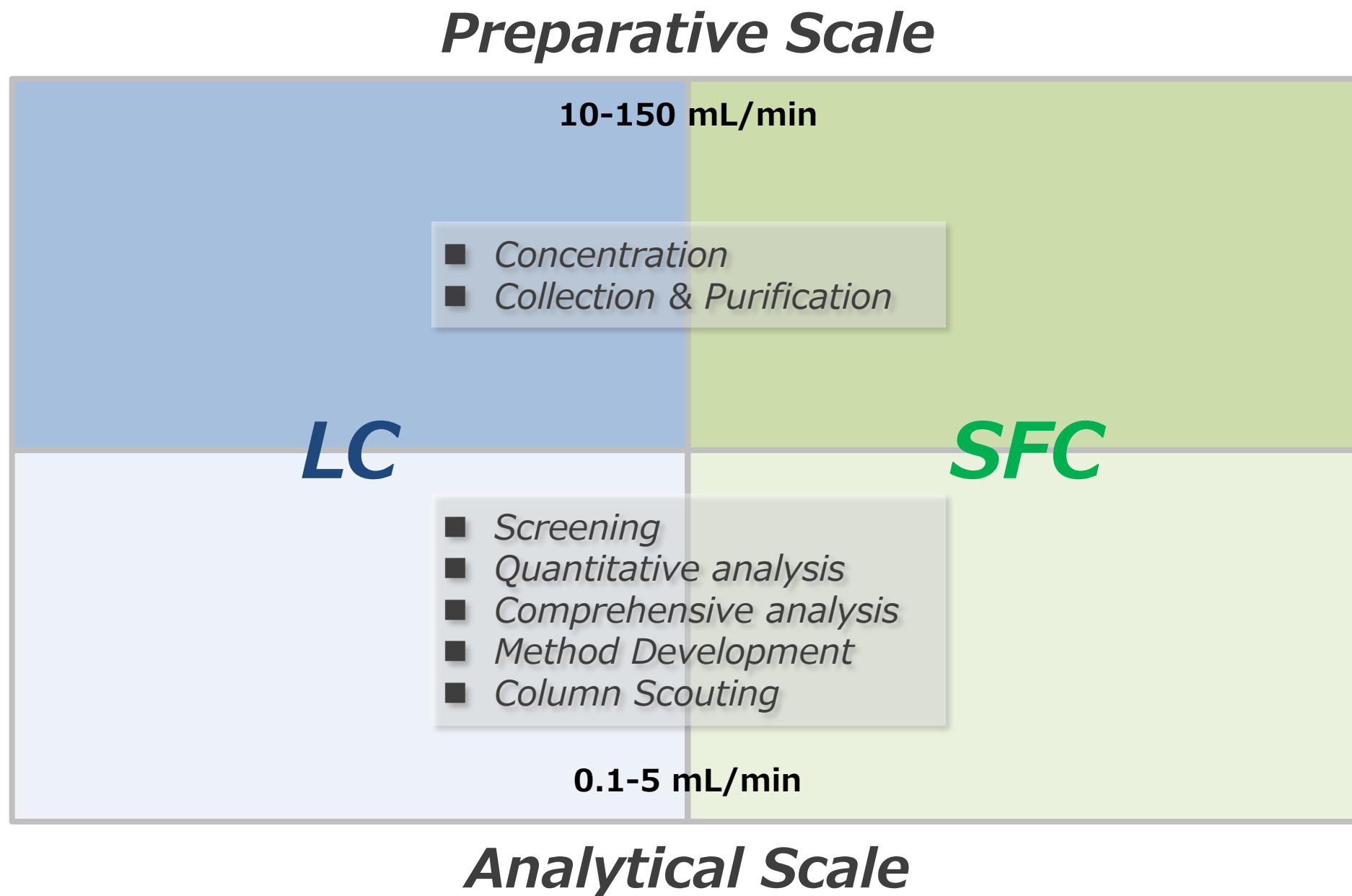
Shimadzu Has Over-40-year LC History

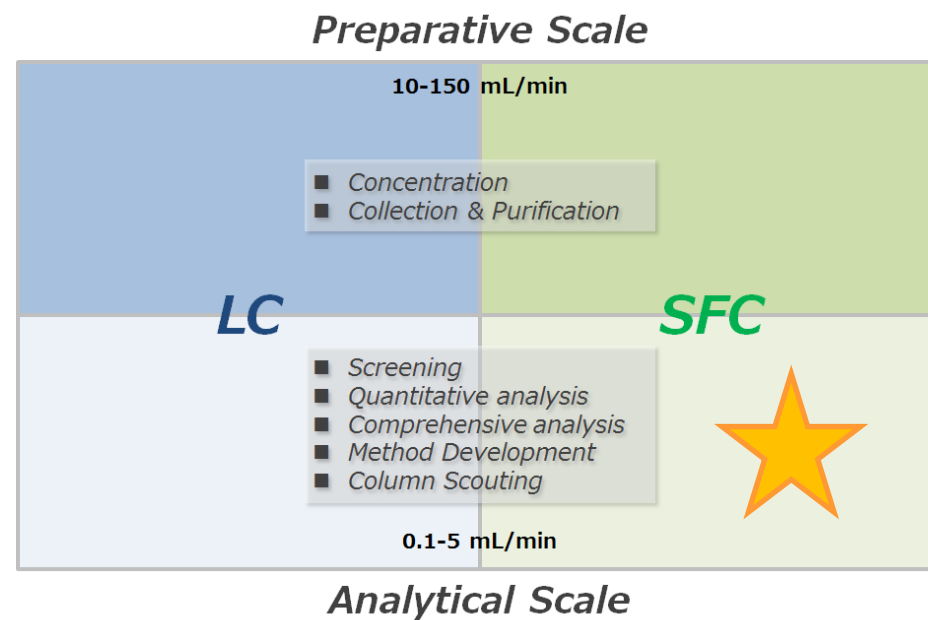
- Prominent hardware performance based on over-40-year-accumulated technology is Shimadzu's pride.

*The culmination
of 41-year history*



What's your purpose?

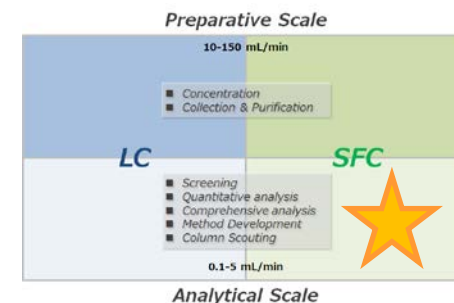




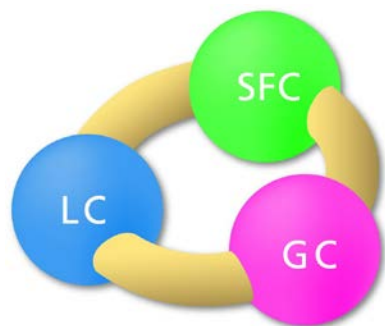
2) Analytical SFC

Nexera UC

Nexera UC
Unified Chromatography

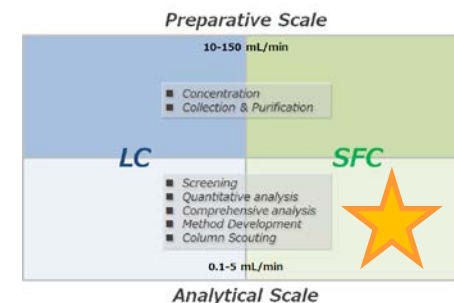


**Unified
Chromatography**



Nexera UC for analysis

- Wide variety of the system configuration.



Online SFE-SFC (-MS) system

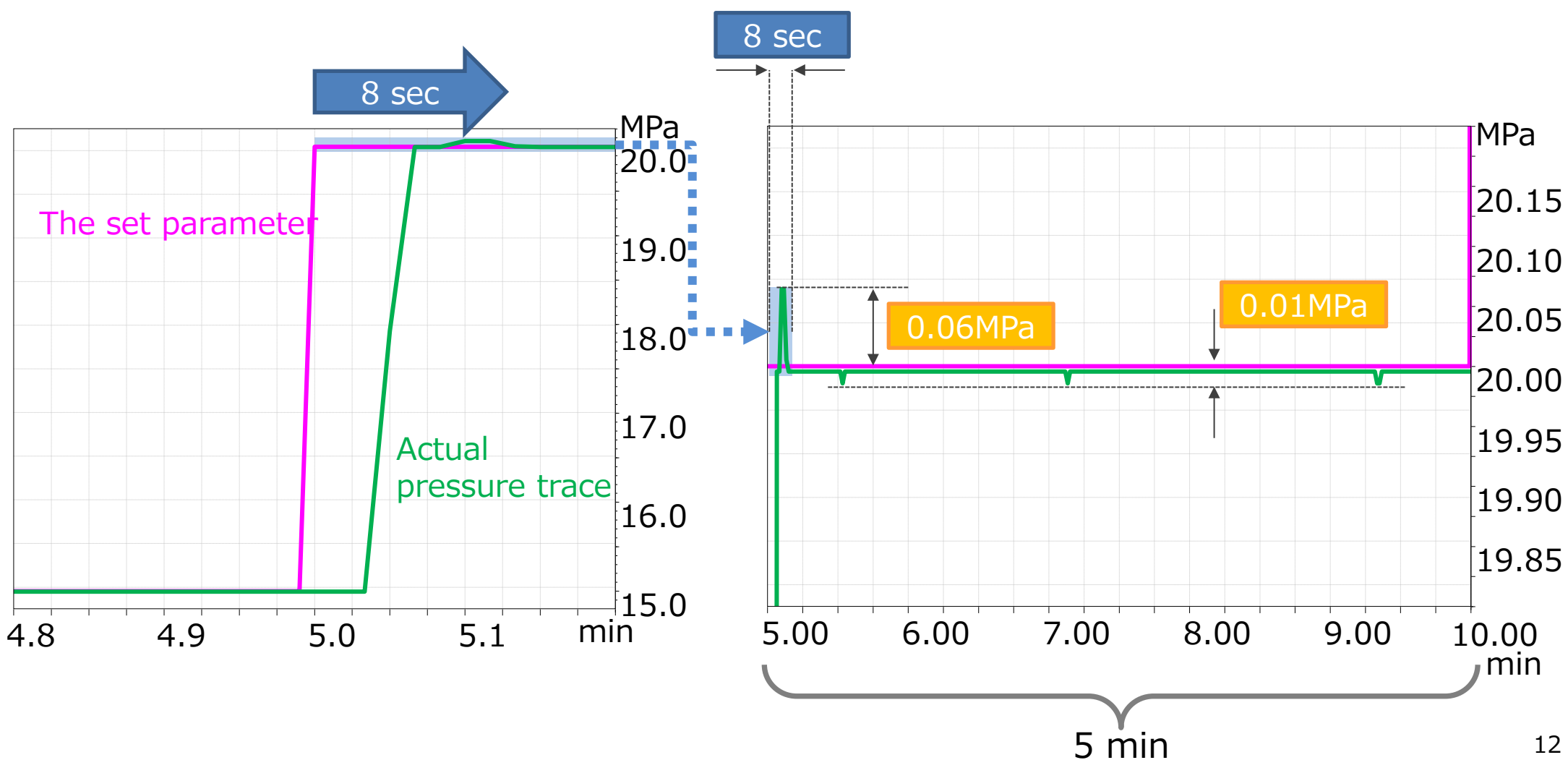


SFE System

SFC (-MS) system

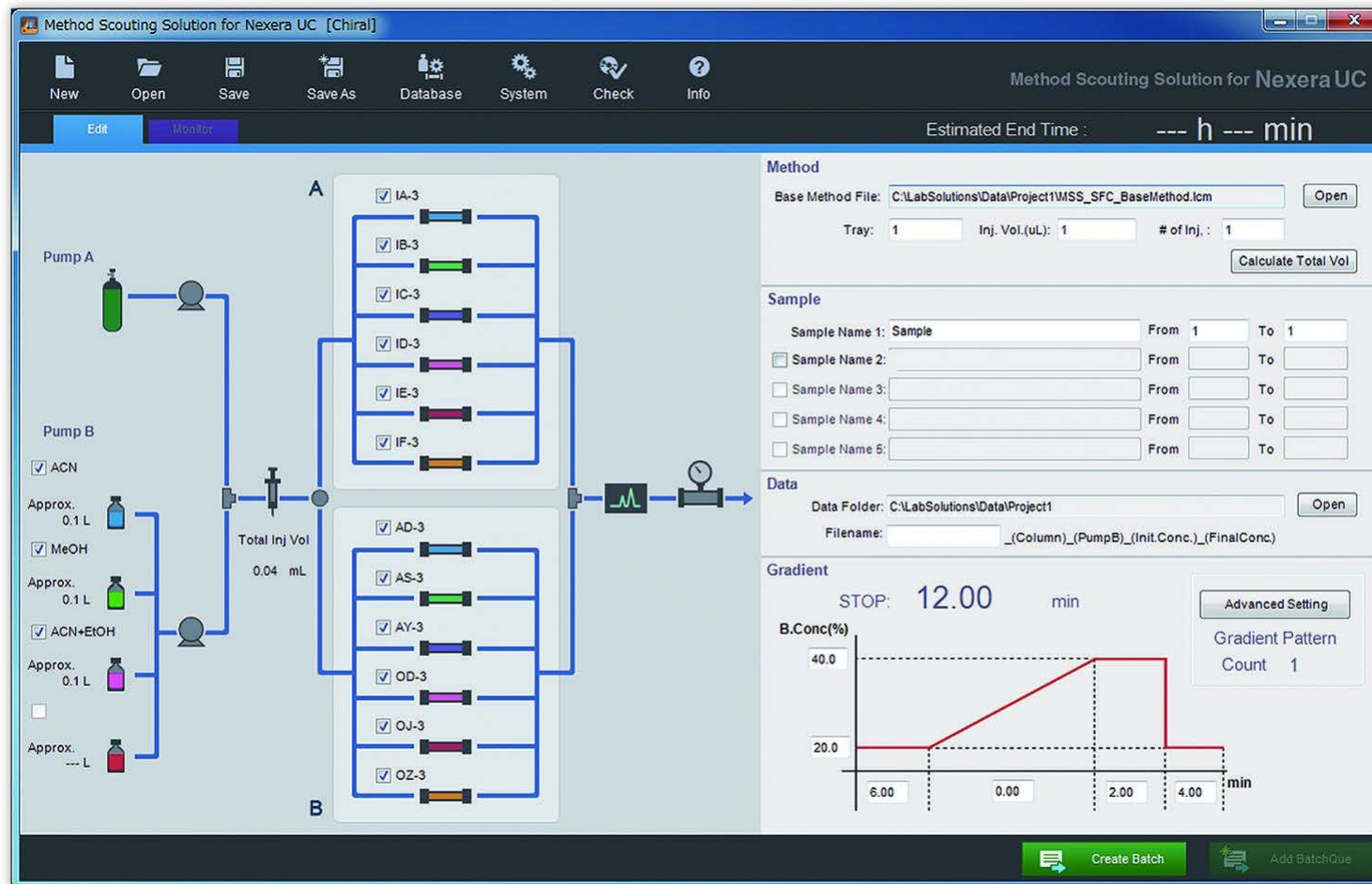
SFC (-MS) system

- Quick response and superior stability of the pressure control.



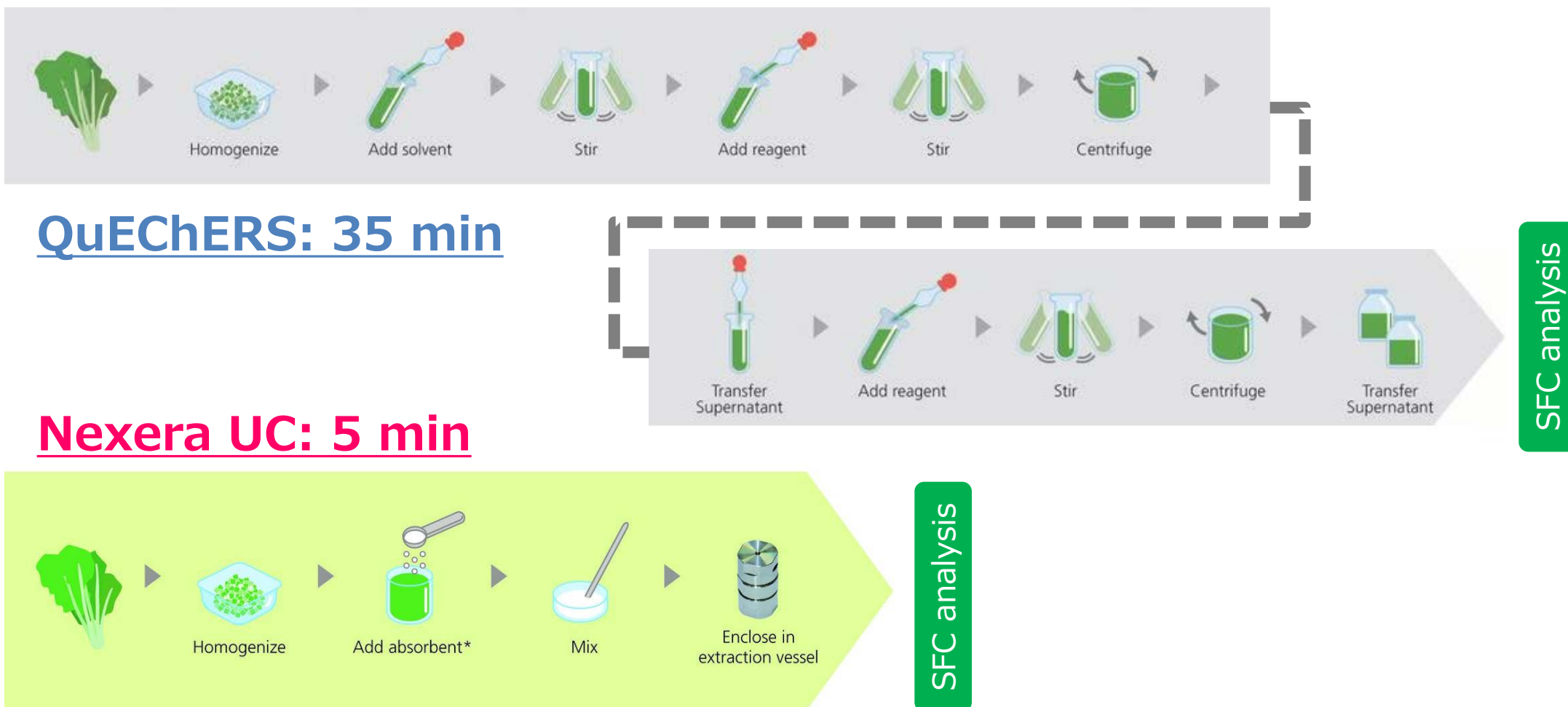
Easy and efficient method scouting

- Method scouting software on LabSolution boosts the workflow of method optimization.



Online SFE system

- The online SFE-SFC system achieves fully automated sample preparation and analysis and improves the work efficiency.



* "Miyazaki Hydro-Protect", Patented in Japan No. 3645552

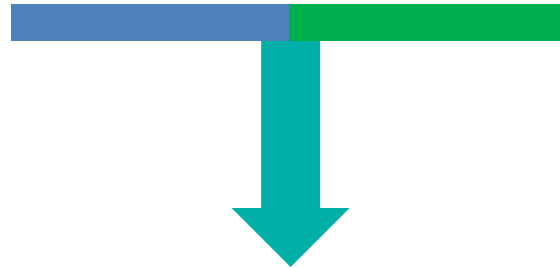
LC & SFC: Nexera UC/s

- Able to be used as UHPLC system or SFC system depending on the demand.



UHPLC system

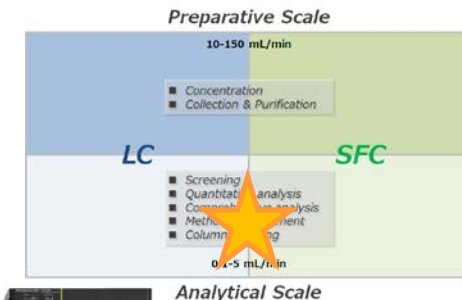
Integration of **LC** & **SFC**
into a single platform



SFC system

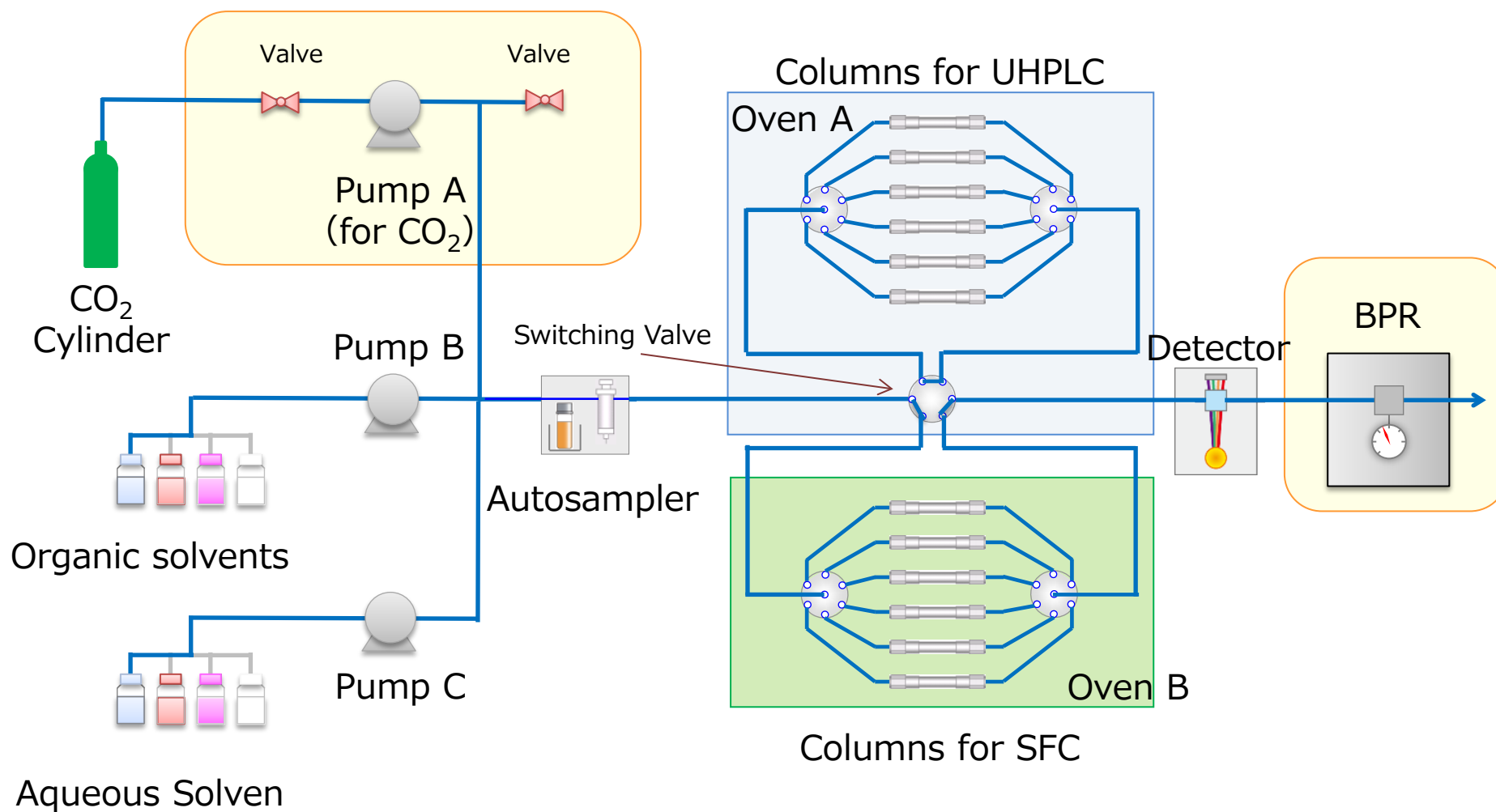


LC/SFC switching system
Nexera UC/s



Nexera UC/s flow diagram

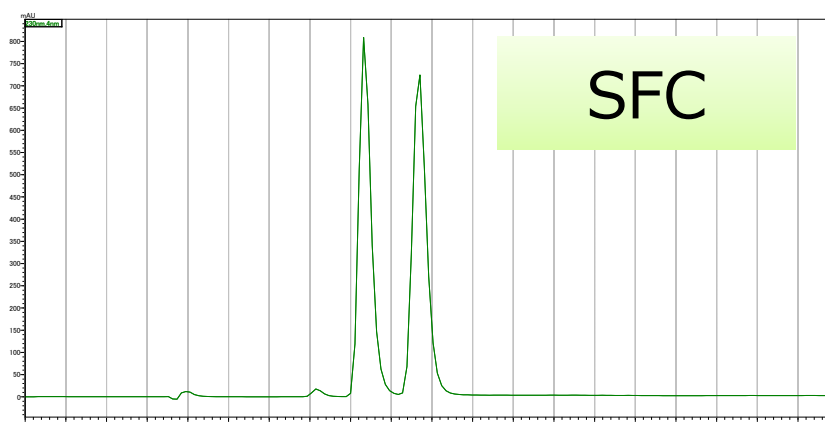
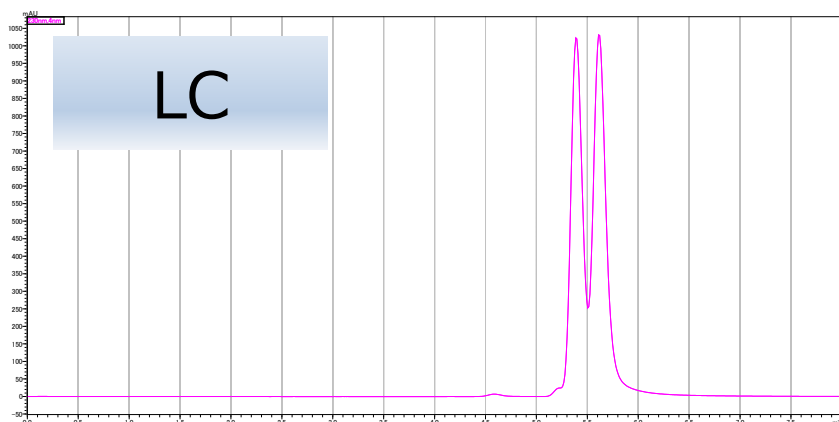
- The flow line is able to be switched by the valve.



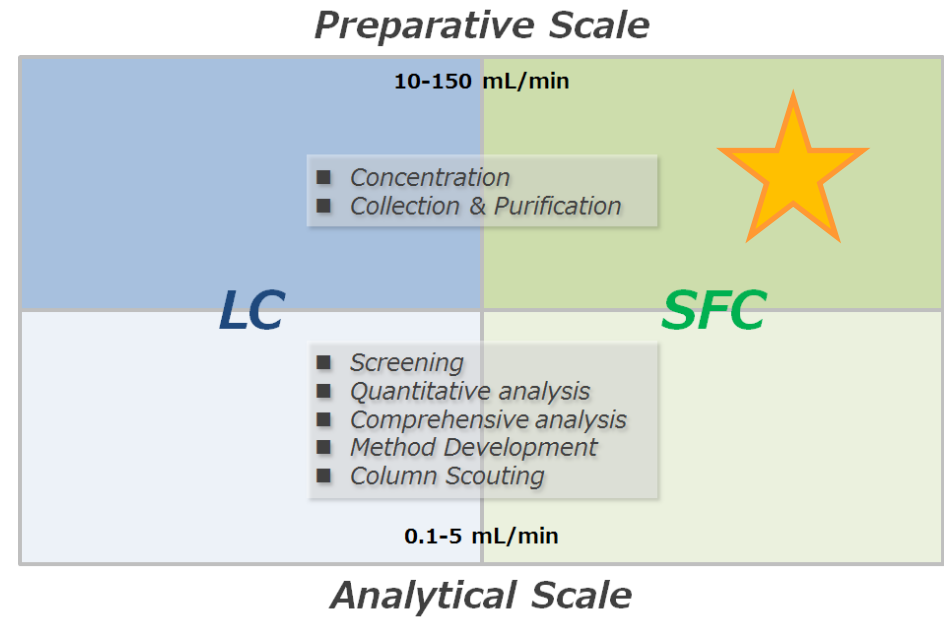
Nexera UC/s flow diagram

- Both LC and SFC are available on the same platform.

Chromatograms of trans-Stilbene Oxide



	LC Conditions	SFC Conditions
Column	CHIRALPAK IC-3 (3 μ m, 4.6 mm \times 150 mm)	CHIRALPAK IC-3/SFC (3 μ m, 4.6 mm \times 50 mm)
Temp	40 $^{\circ}$ C	40 $^{\circ}$ C
Mobile phase A	None	CO ₂
Mobile phase B	MeOH	MeOH
Mobile phase C	10 mmol/L NH ₄ HCO ₃ aq.	None
Mising ratio	85% B	5% B
Flow rate	0.5 mL/min	2.0 mL/min
Pressire on BPR	None	12 MPa



3) Semi-Preparative SFC

Collaboration with ETC

1



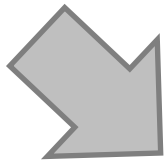
Demands by ETC members
-> the H/W & S/W specification

3

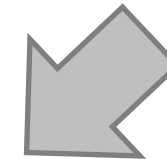
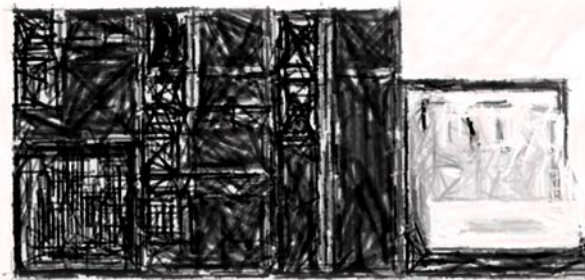
Need to be improved

- ☐ Usability
- ☐ Robustness
- ☒ Recovery
- ☒ Size
- ☐ Performance etc...

Evaluation by ETC members

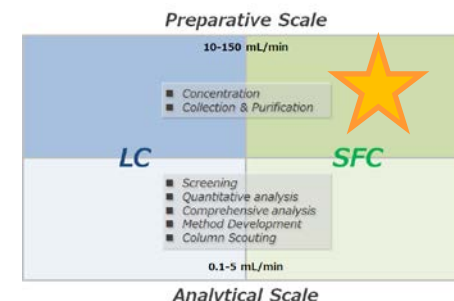


2



Shimadzu designed the prototype
of H/W & S/W

Nexera UC Prep



*Unparalleled performance,
unparalleled flexibility*

- **LotusStream** achieves higher recovery
- Simple operation
- Compact, benchtop design
- SFC analysis system + Fraction collector

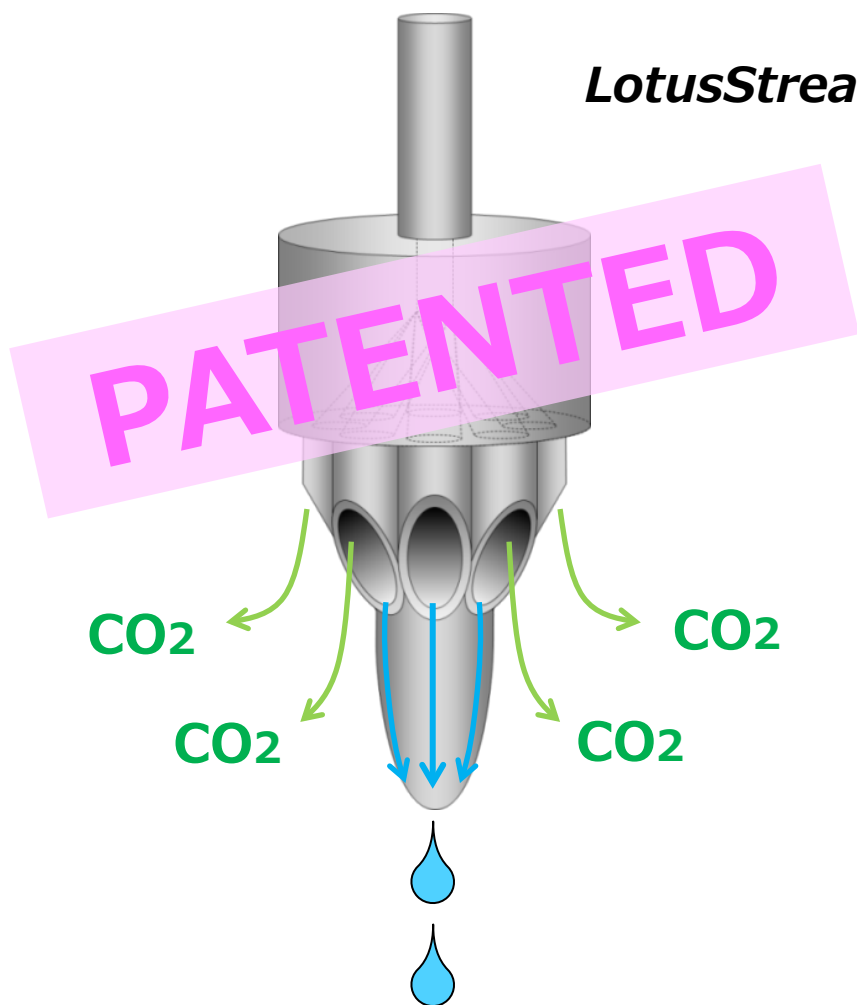


Why the lotus?



Excellent recovery ratio

- LotusStream technology provides a superior recovery ratio by preventing spray of the elution.



LotusStream separator

Comparison for 1% linalool

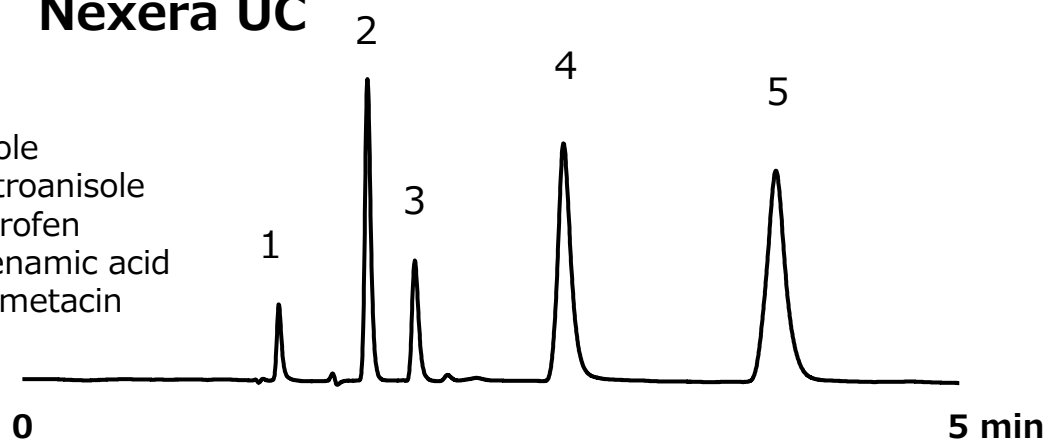
Equipment	Recovery rate
Regular nozzle	78.0%
LotusStream separator	96.7%

Smooth scale-up procedure

Nexera UC

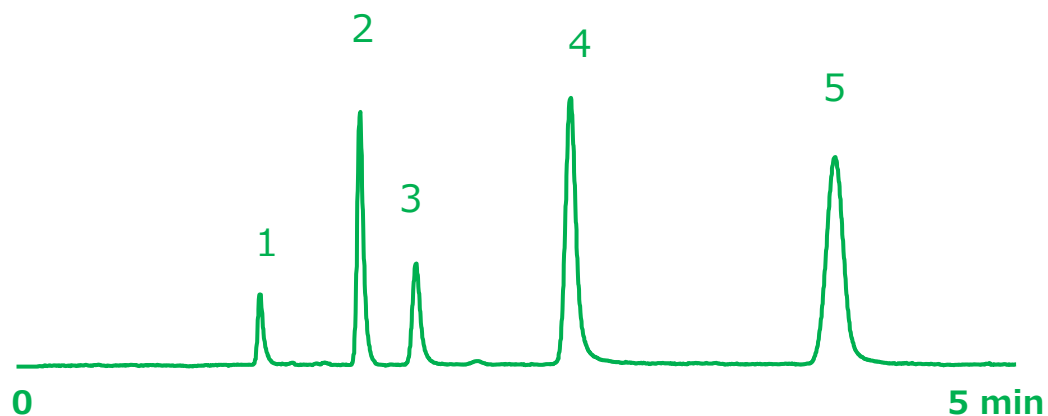
Peaks:

1. Anisole
2. p-Nitroanisole
3. Ibuprofen
4. Tolfenamic acid
5. Indometacin



Flow rate : 3 mL/min
Mobile phase: CO₂ / MeOH = 90/10
Column : 250 x 4.6 mm, 5μm, Diol
Temp. : 40 °C
Pressure : 10MPa
Injection : 0.1 μL

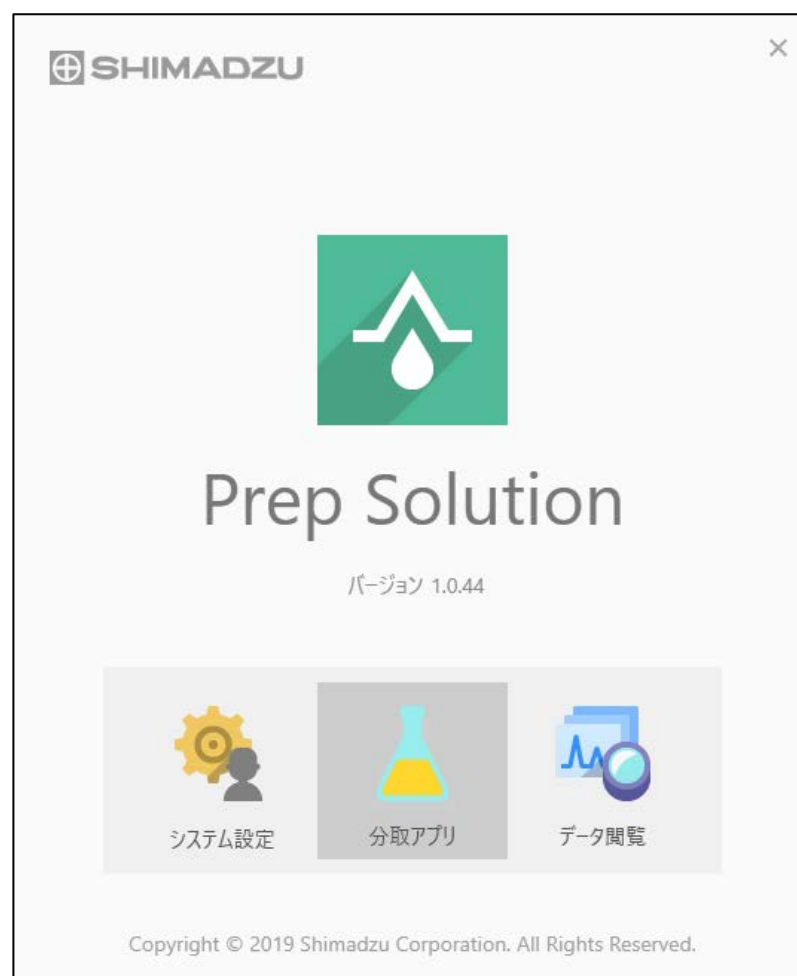
Nexera UC Prep



Flow rate : 60 mL/min
Mobile phase: CO₂ / MeOH = 90/10
Column : 250 x 20 mm, 5μm, Diol
Temp. : 40 °C
Pressure : 10MPa
Injection : 50 μL

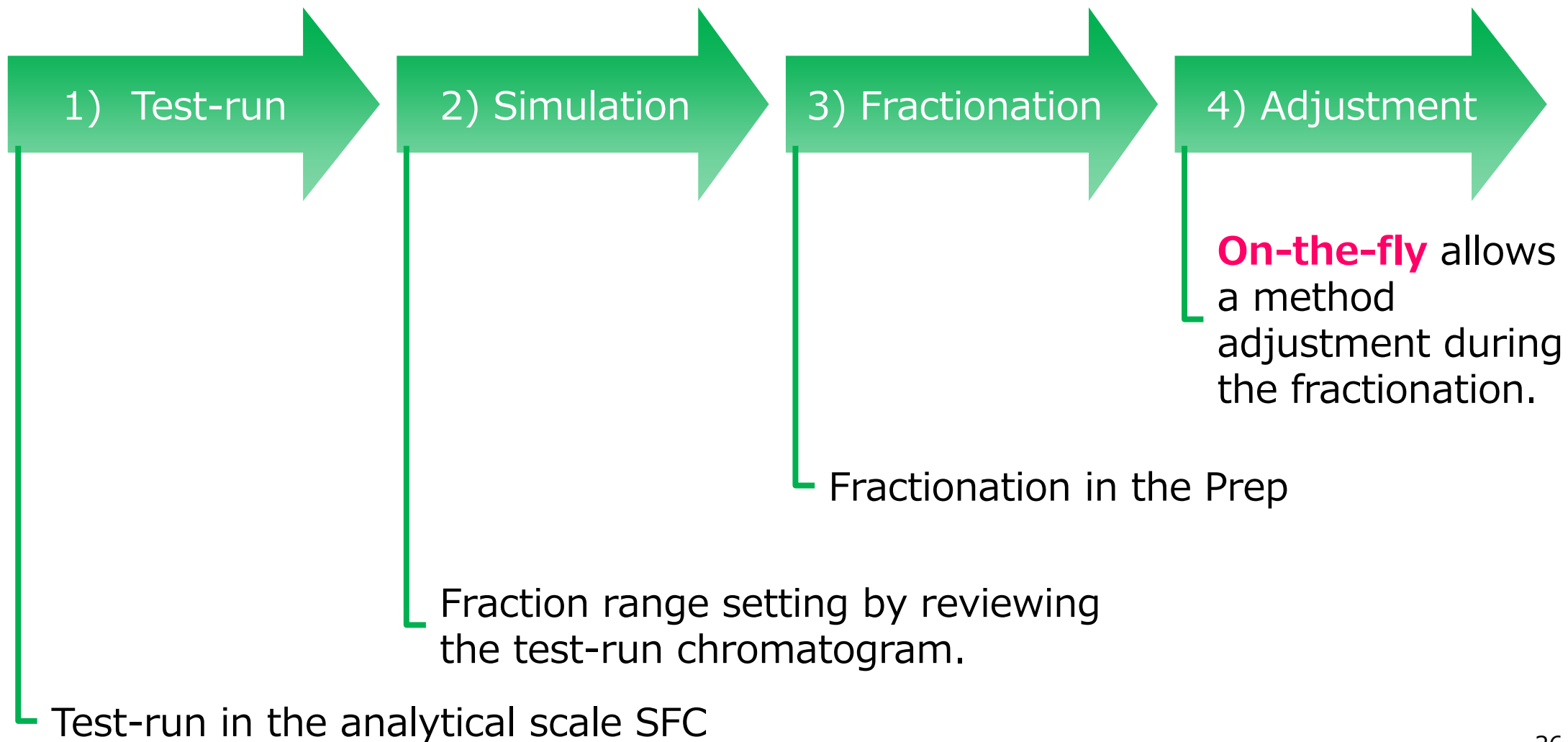
Smooth scale-up procedure

- Scale-up from the analytical size to the preparative size is smooth on [Prep Solution](#) based on LabSolution.



Smooth scale-up procedure

- Scale-up from the analytical size to the preparative size is smooth on [Prep Solution](#) based on LabSolution.

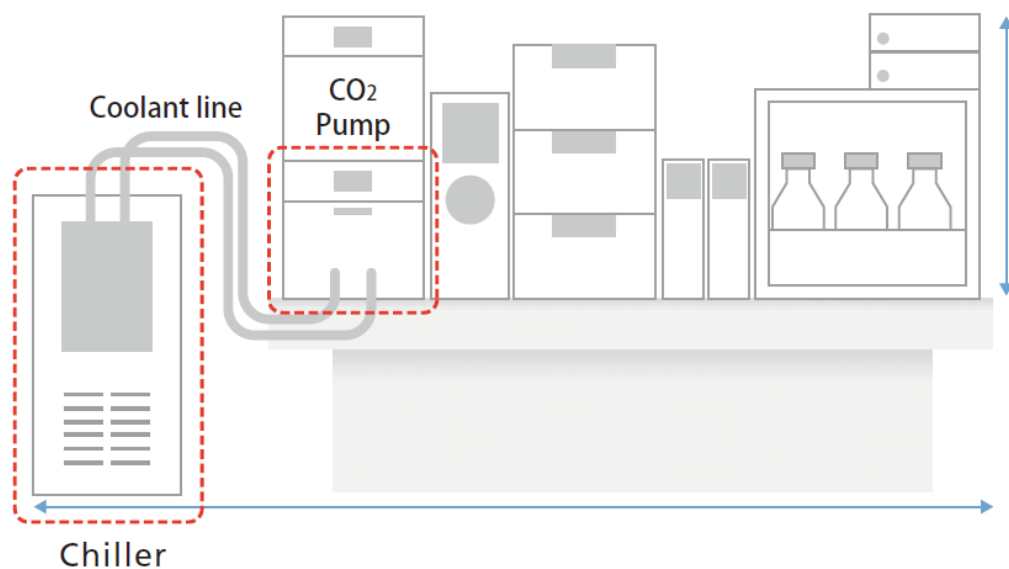


Smooth scale-up procedure



Benchtop design

- No chiller on the floor anymore. Everything is integrated in the system on the bench, contributing to a smaller installation space.



Traditional preparative SFC system

Footprint is
reduced by
40%



Nexera UC Prep

Analytical system -> Prep system

- Test separation on the analytical scale -> move to the appropriate option of preparative LC or SFC.

Preparative LC system
Nexera Prep



LC/SFC switching system
Nexera UC/s



SCALE-UP



Preparative SFC system
Nexera UC Prep



Analytical system -> Prep system

- Test separation on the analytical scale -> move to the appropriate option of preparative LC or SFC.

Preparative LC system
Nexera Prep



LC/SFC switching system
Nexera UC/s



SCALE-UP



Preparative SFC system
Nexera UC Prep



Chiral or Comprehensive?

- Two types of systems are available depends on your purpose.

Stacked Fraction Purification System



- Collects several kinds of the targeted component in large scale
- The combination with stack injection improves the productivity

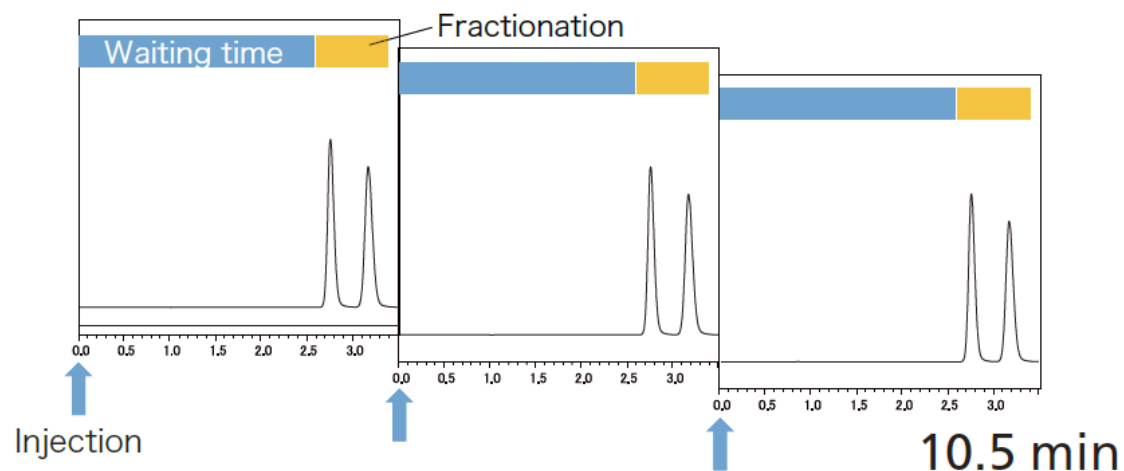
Multi-Fraction Purification System



- Collects multiple fractions comprehensively
- The collection volume is small, but many fractions including the impurities are collected

Stack injection

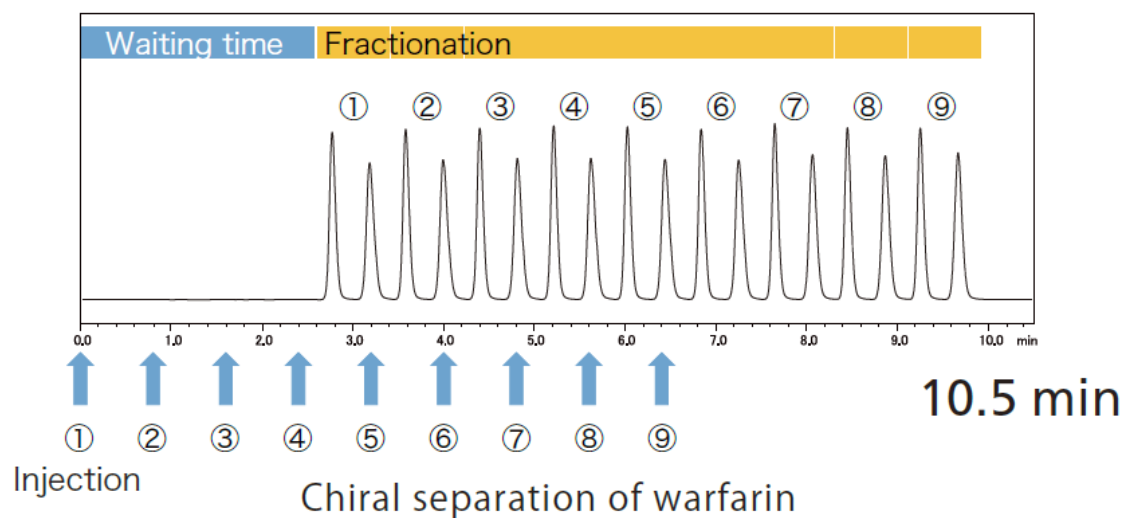
Normal injection



3 injections

3x more injections!

Stacked injection (9 consecutive injections)



9 injections

Analytical SFC also becomes preparative SFC

- Even the analytical SFC system can be directly used as the small scale prep system by adding the fraction collector.



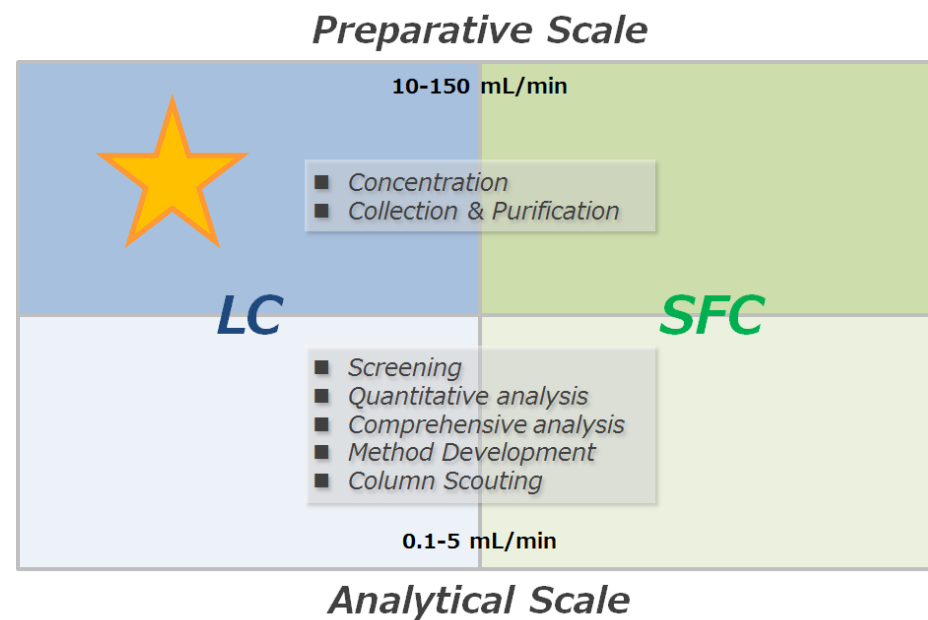
Analytical SFC system
Nexera UC



Small scale prep SFC

Typical max. load (one injection in a 250 mm column)

Nexera UC		Nexera UC Prep	
20 mg	100 mg	500 mg	1 g
4.6 mm I.D.	10 mm I.D.	20 mm I.D.	30 mm I.D.



4) Preparative LC

Preparative LC is also available

- Preparative Lc “Nexera Prep” is also available in the same workflow.

Preparative LC system
Nexera Prep



LC/SFC switching system
Nexera UC/s

LC is preferable

SCALE-UP

SFC is preferable

Preparative SFC system
Nexera UC Prep



Preparative LC is also available

- Preparative Lc “Nexera Prep” is also available in the same workflow.

Preparative LC system
Nexera Prep



LC/SFC switching system
Nexera UC/s

LC is preferable

SCALE-UP

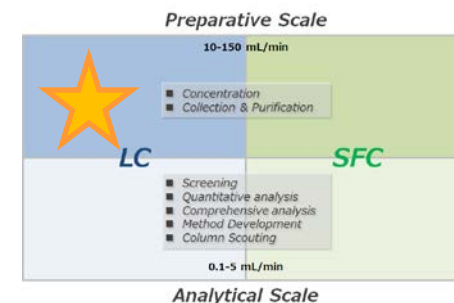
SFC is preferable

Preparative SFC system
Nexera UC Prep



Nexera Prep lineup

- Wide variety of configuration fulfills any demands.



Preparative LCMS system



Purity check system



Be simple.
Be flexible.

UFPLC system



Multi fraction collector system



5) Summary and Conclusions

Again, what's your purpose?

Preparative Scale

Nexera Prep



10-150 mL/min

Nexera UC Prep



- Concentration
- Collection & Purification

LC

SFC

Nexera



i-Series



Nexera UC/s

- Screening
- Quantitative analysis
- Comprehensive analysis
- Method Development
- Column Scouting

0.1-5 mL/min

Nexera UC



Analytical Scale

1) Work on SFC from analytical scale to prep scale

Preparative Scale

Nexera Prep



10-150 mL/min

Nexera UC Prep



- Concentration
- Collection & Purification

LC

SFC

Nexera



i-Series



Nexera UC/s

- Screening
- Quantitative analysis
- Comprehensive analysis
- Method Development
- Column Scouting

0.1-5 mL/min

Nexera UC



Analytical Scale

2) Work on SFC and LC for analytical purpose

Preparative Scale

Nexera Prep



10-150 mL/min

- Concentration
- Collection & Purification

Nexera UC Prep



LC

Nexera



i-Series



Nexera UC/s

- Screening
- Quantitative analysis
- Comprehensive analysis
- Method Development
- Column Scouting

0.1-5 mL/min

SFC

Nexera UC



Analytical Scale

3) Preparative work in multiple means

Preparative Scale

Nexera Prep



10-150 mL/min

- Concentration
- Collection & Purification

Nexera UC Prep



LC

SFC

Nexera UC/s

Nexera

i-Series



- Screening
- Quantitative analysis
- Comprehensive analysis
- Method Development
- Column Scouting

Nexera UC



0.1-5 mL/min

Analytical Scale

4) Work on LC from analytical scale to prep scale

Preparative Scale

Nexera Prep



10-150 mL/min

Nexera UC Prep



- Concentration
- Collection & Purification

LC

SFC

Nexera



i-Series



Nexera UC/s

- Screening
- Quantitative analysis
- Comprehensive analysis
- Method Development
- Column Scouting

0.1-5 mL/min

Nexera UC



Analytical Scale

Well, how about the software?

Preparative Scale

Nexera Prep 10-150 mL/min Nexera UC Prep

LC *SFC*

Nexera i-Series

Screening
Quantitative analysis
Comprehensive analysis

Nexera UC

0.1-5 mL/min

Analytical Scale

LabSolutions controls everything!

The diagram illustrates the range of Shimadzu chromatography systems controlled by LabSolutions software. It is organized into two main sections: Preparative Scale and Analytical Scale. The Preparative Scale section at the top features Nexera Prep and Nexera UC Prep systems, operating at flow rates of 10-150 mL/min. The Analytical Scale section at the bottom features Nexera, i-Series, and Nexera UC systems, operating at flow rates of 0.1-5 mL/min. A central LabSolutions software box, displaying a chromatogram, is positioned between the two scales. A pink banner at the bottom of the diagram emphasizes that LabSolutions controls everything.

Take-home message

- We present Shimadzu products related to;
 - SFC & LC,
 - from analytical through preparative works,
 - controlled by the single software.
- The unique technology “LotusStream” improves the recovery ratio significantly.



