International collaborative research project

"Paper-Based Sensor Devices for Rapid and Accurate Detection of COVID-19"

Tsuyoshi MINAMI[1] and Anthony GENOT[1, 2]

1. Institute of Industrial Science, The University of Tokyo

2. French National Centre for Scientific Research (CNRS)

International Collaborative Research with France

Genot group (France)

Development of materials for RNA detection

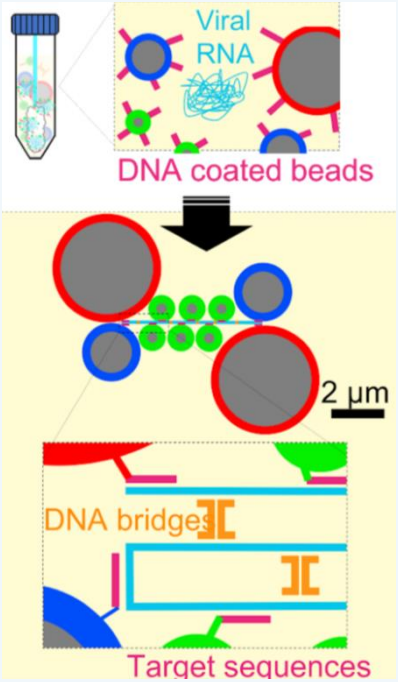
Collaboration

Minami group (Japan)

Establishment of paper-based array and image analysis

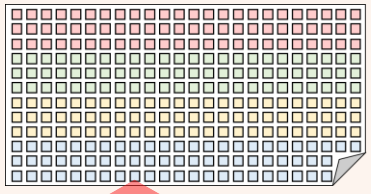
Development of a rapid detection method for RNA

RNA detection

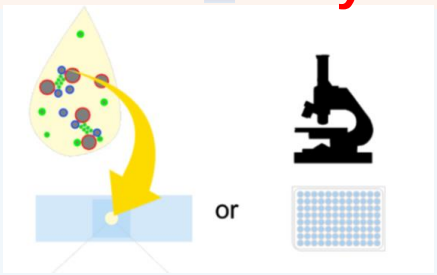


feedback

Disposable paper-based sensor array

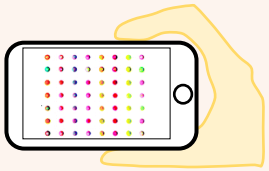


This study



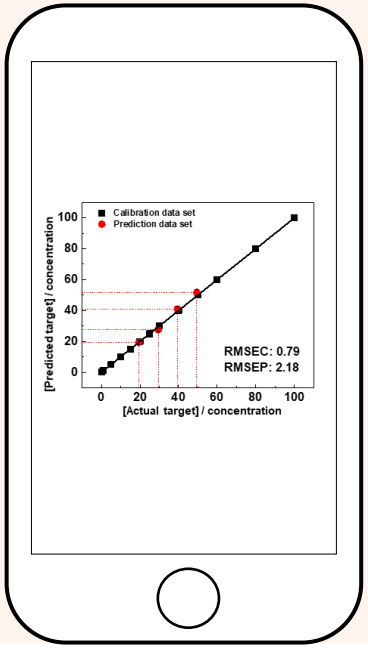
Conventional method

Data collection by CCD camera or smartphone



Diagnosis

(Future work) Development of App.



ANR Flash call covid-19

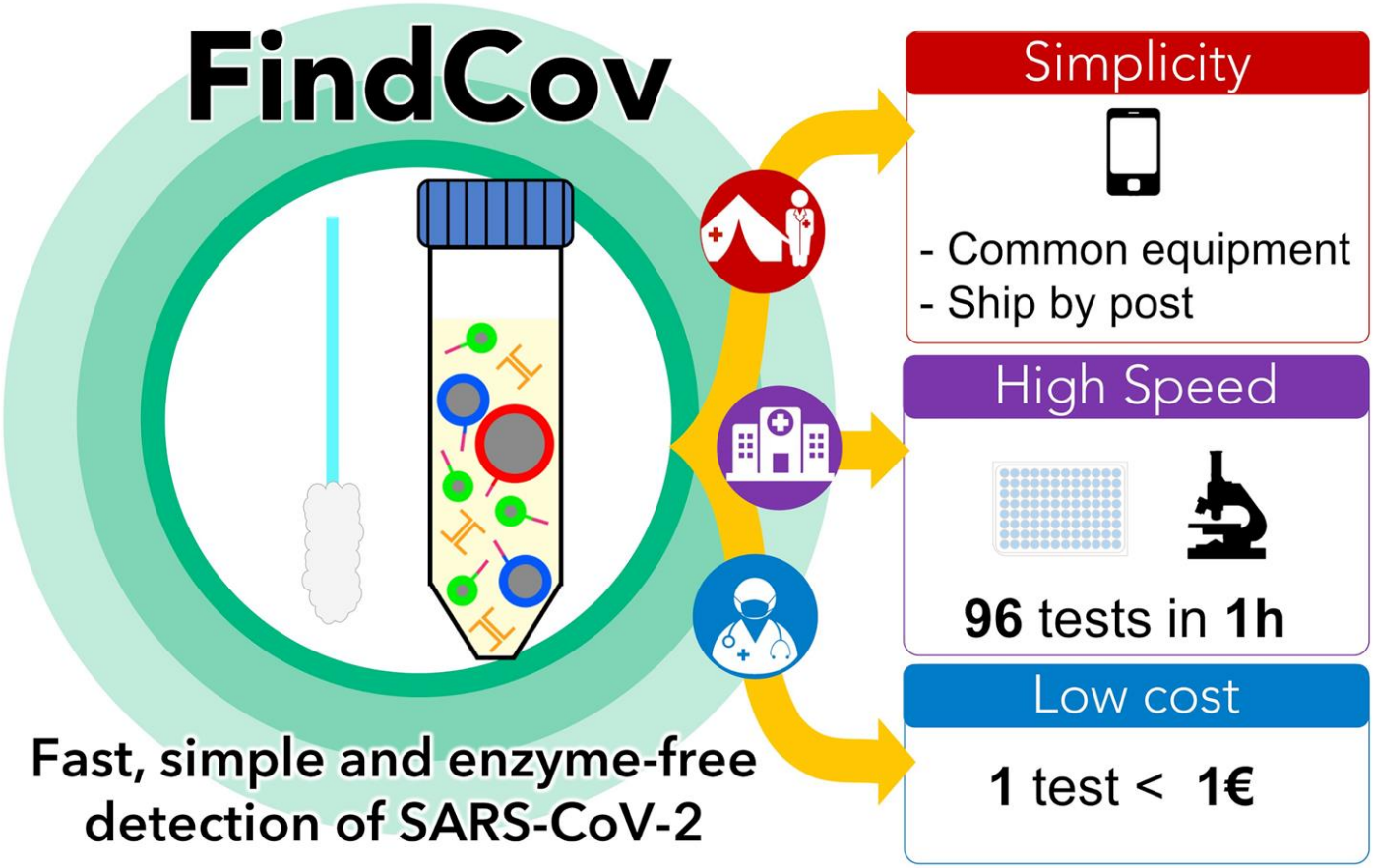
- The french National Agency for Research (ANR) opened a flash call on covid-19 in March.

- Budget initially 2M€, increased to 14.5 M€
- 279 applications , 86 projects selected
- Collaboration with various research fields （ex. engineering, biology, medicine, mathematics, ethics, sociology, and law, etc.）

Examples of themes:

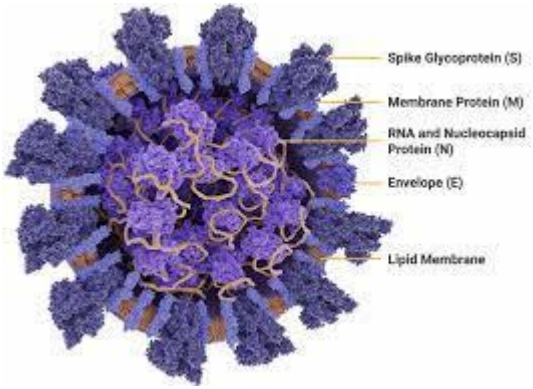
- preventive measures
- treatments, including vaccines
- large-scale testing
- seroprevalence studies
- epidemiological rebounds
- unlocking strategies

Our project



Goal: Establishment of a rapid, simple and enzyme-free detection method for SARS-Cov2

Covid-19



promega.jp

Features

- Long incubation time
- Many asymptomatic carriers

Li et al., Science 2020.

Massive testing neeeded

JUNG YEON-JE | AFP

In South Korea

- test approved in a few days
- ~20,000 tests/day
- Contact tracing

Massive shortage of tests

Biotechnology

Why the CDC botched its coronavirus testing

The first testing kits from the Centers for Disease Control had a simple fault, and red tape prevented other labs from creating their own.

by **Neel V. Patel** March 5, 2020

Coronavirus: White House concedes US lacks enough test kits

6 March 2020 Share

Coronavirus pandemic

Reasons

- Lack of reagents
- Lack of manpower
- Cost
- Reliability

Limitations of PCR (and enzymatic methods)

Swab Collection → RNA extraction from sample → Reverse Transcription → Amplification of cDNA → Readout

Shortage of extraction kits

Tweeter

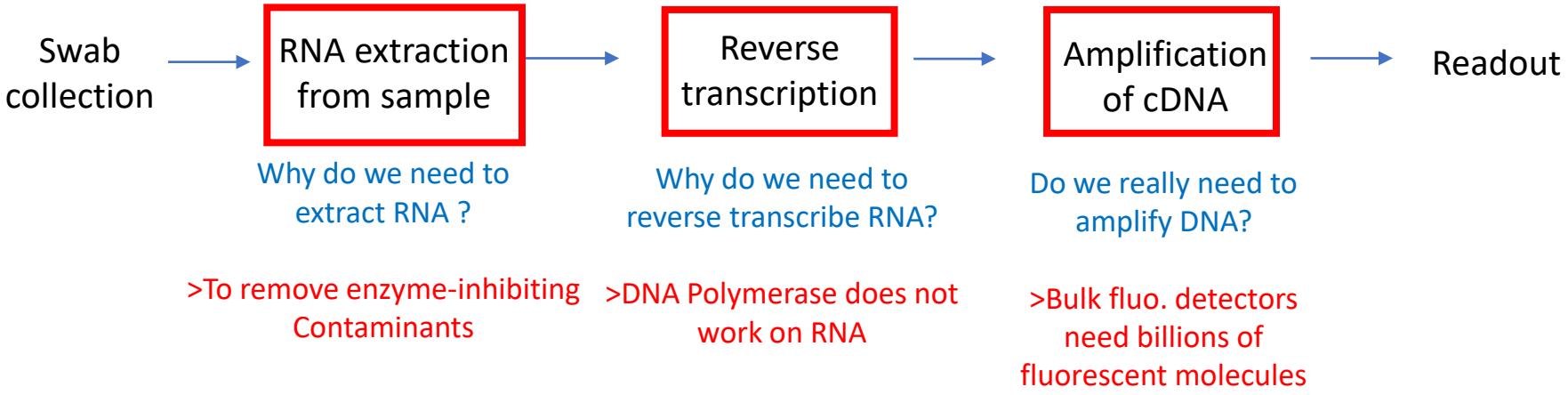
Needs enzymes

takarabio.com

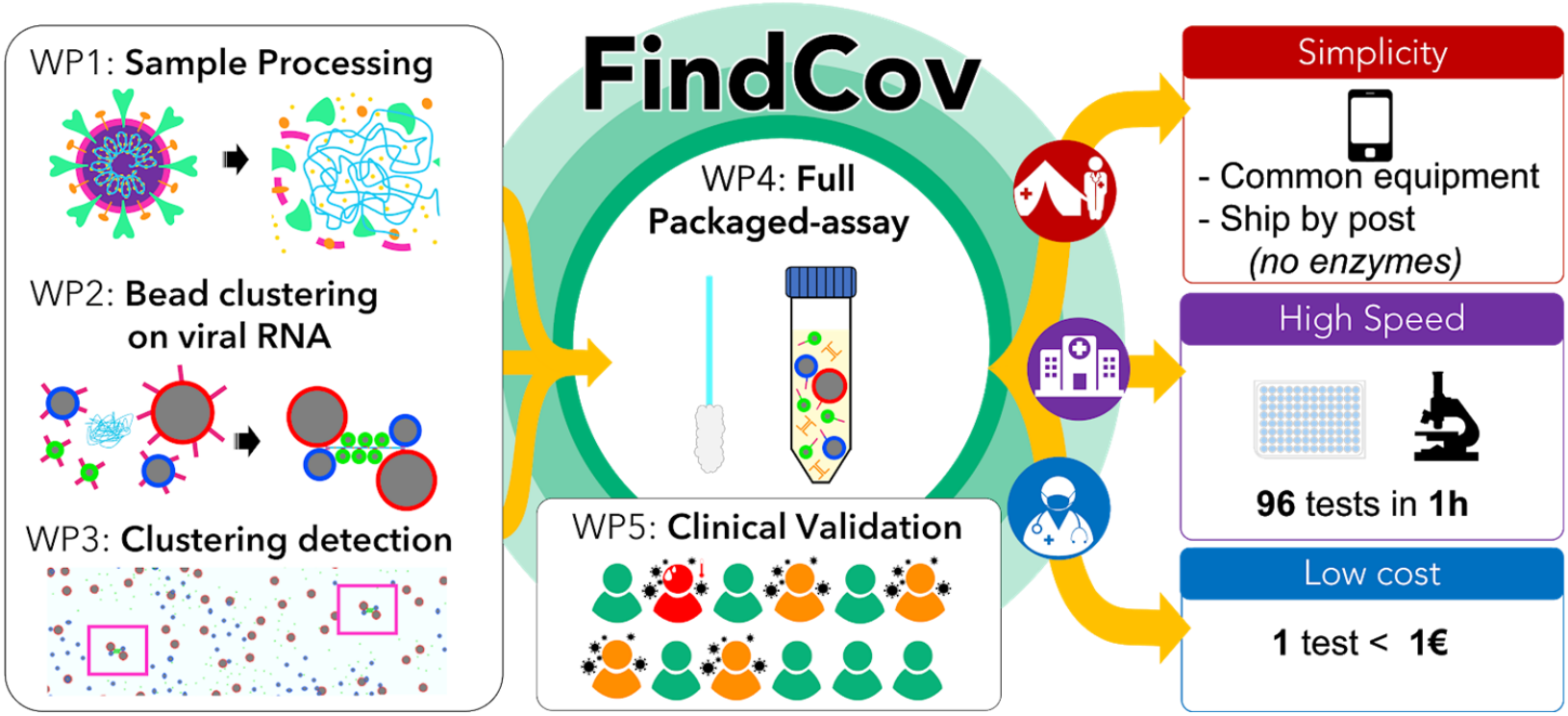
Needs device for temperature cylcing and fluorescence reading

Biorad.com

Can we do differently ?



The community of immuno assays has detected proteins for 50 years without all this !


WP1: Sample Processing
WP2: Bead clustering on viral RNA
WP3: Clustering detection
FindCov
WP4: Full Packaged-assay
WP5: Clinical Validation
Simplicity
- Common equipment
- Ship by post
(no enzymes)
High Speed
96 tests in 1h
Low cost
1 test < 1€

ANR Flash FindCov project

Simple, fast and enzyme-free detection of SARS-Cov-2

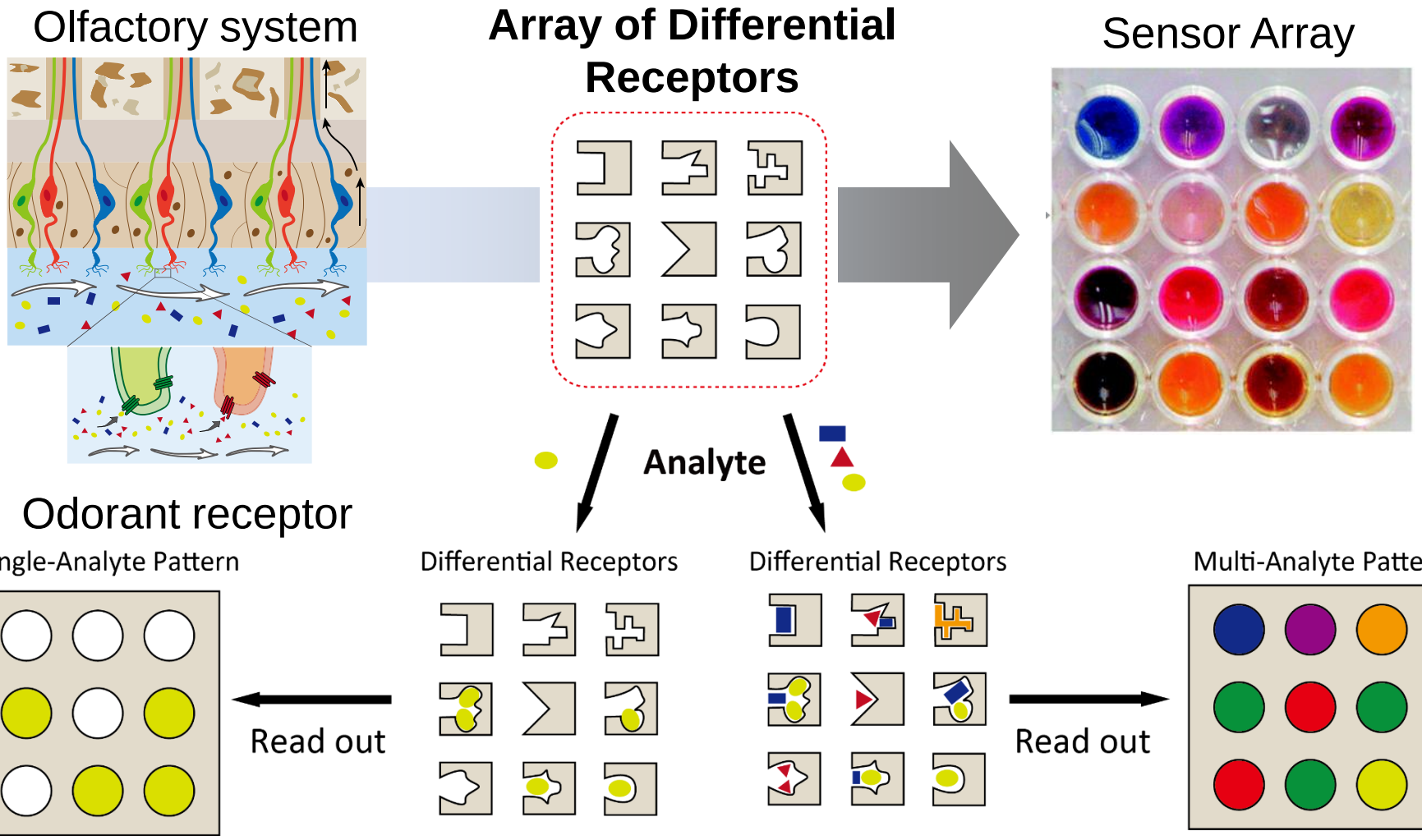
Deteix
Genot
Lobato
Okumura
Roy

Tauran

Gines
Rondelez

Fujii
Minami
Sasaki
Kubota
Xiaojun

Chemosensor Array



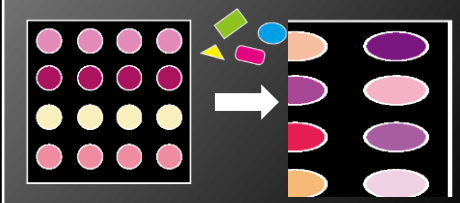
K. Suslick et al., *Nature* **2000**, 406; E. V. Anslyn et al., *Angew. Chem. Int. Ed*. **2001**, *40*, 3118; T. Minami et al., *J. Am. Chem. Soc.* **2013**, *135*, 15238; T. Minami et al., *Coord. Chem. Rev.* **2021**, *429*, 213607.

Chemosensor arrays can achieve high-throughput sensing in combination with pattern recognition algorithms.

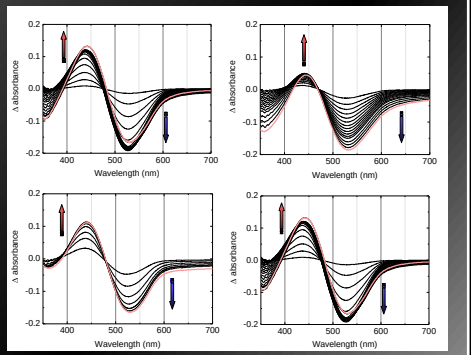
Chemometrics for Analytical Chemistry

Data collection

Sensing



Recording



Making Matrix

	Sensor 1			Sensor 2			Sensor *m*		
	Abs λ_1	Abs λ_2	Abs λ_m	Abs λ_1	Abs λ_2	Abs λ_m	Abs λ_1	Abs λ_2	Abs λ_m
Control									
Trial 1									
Trial 2									
Trial *n*									
Analyte 1									
Trial 1									
Trial 2									
Trial *n*									
Analyte *m*									
Trial 1									
Trial 2									
Trial *n*									

Multi-dimensional dataset

Input

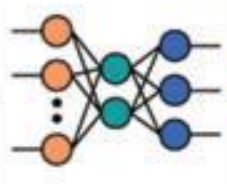
Data analysis

Preprocessing

Student's t-test
Outlier detection

Feature extraction

Prediction



Classification

Model selection

Hypothesis test

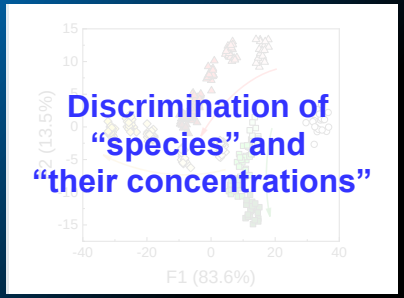
Output

Result

Qualitative assay

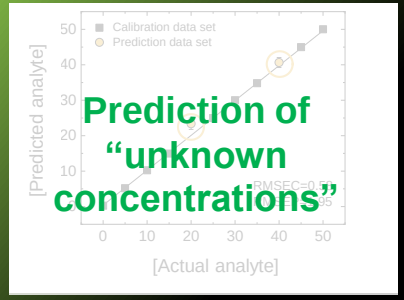
Discrimination of "species"

Semi-quantitative assay



Discrimination of "species" and "their concentrations"

Quantitative assay

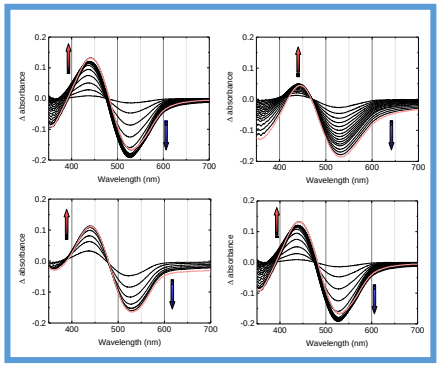


Prediction of "unknown concentrations"

Review see; T. Minami et al., *Coord. Chem. Rev.* **2021**, *429*, 213607.

Outline of the Chemometric Analysis

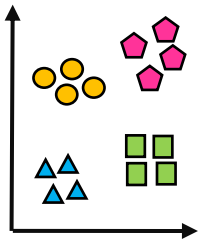
Various Color Change



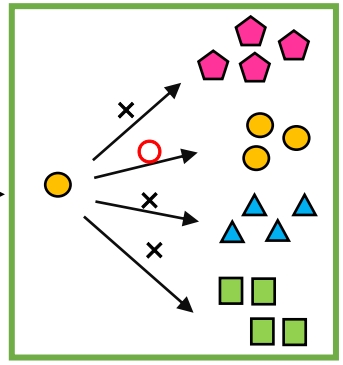
20 repetitions for each analyte

Preprocessing (*e.g.* t-Test)

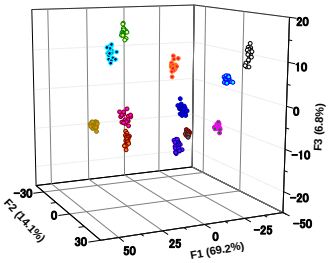
Dimensionality Reduction



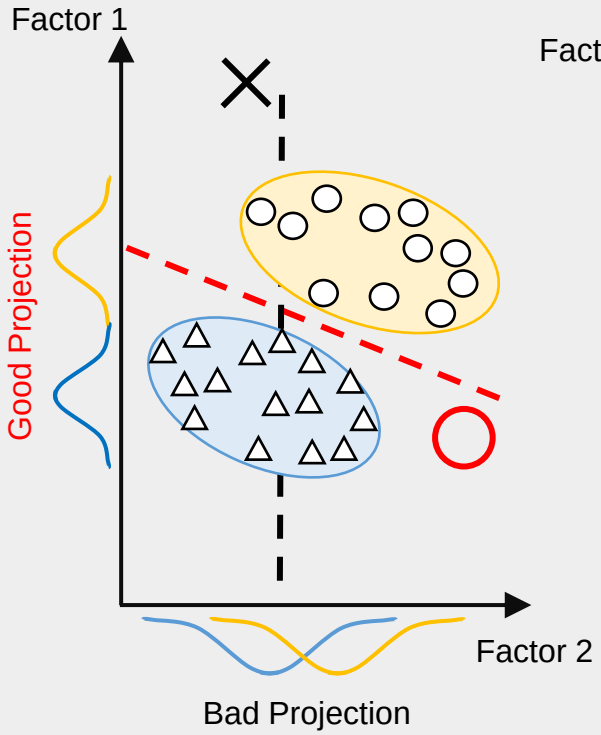
Prediction

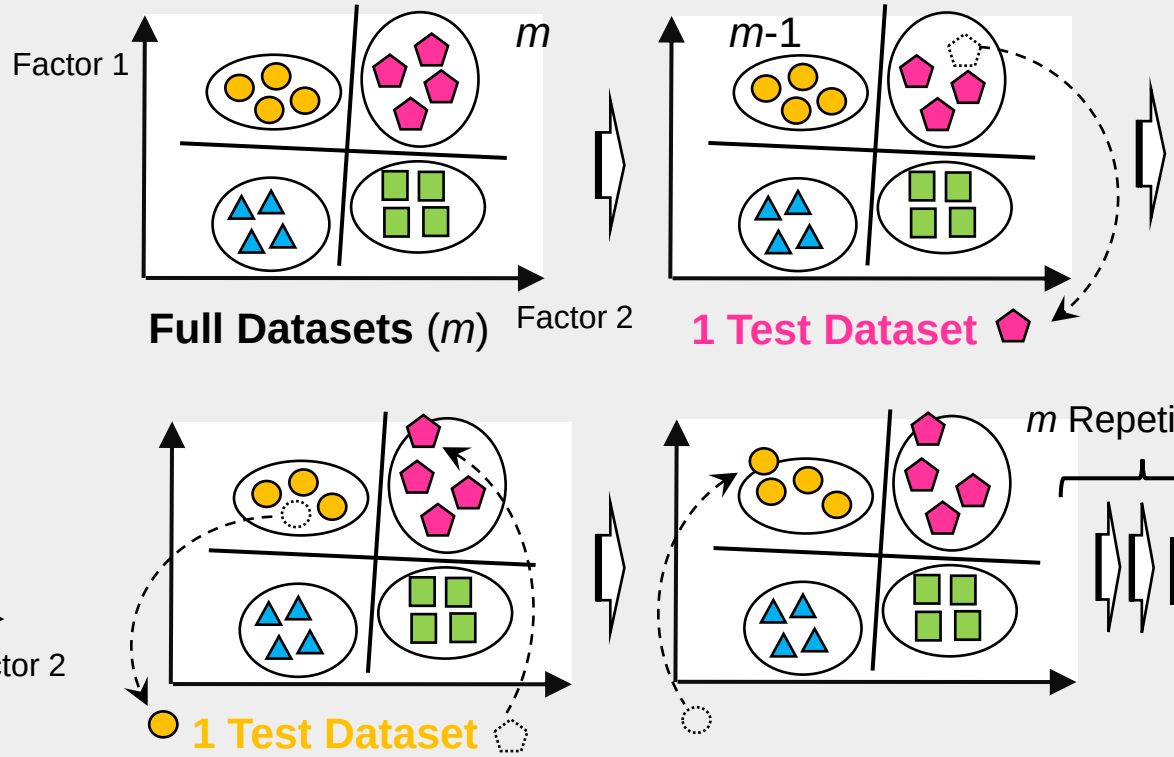


Analysis Result



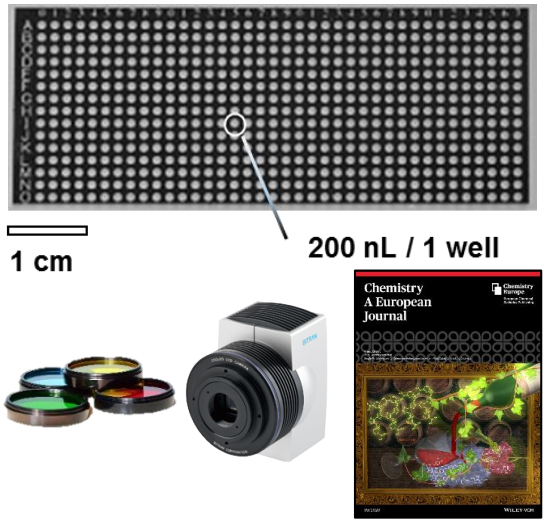
Linear Discriminant Analysis (LDA) with the Jackknife Method



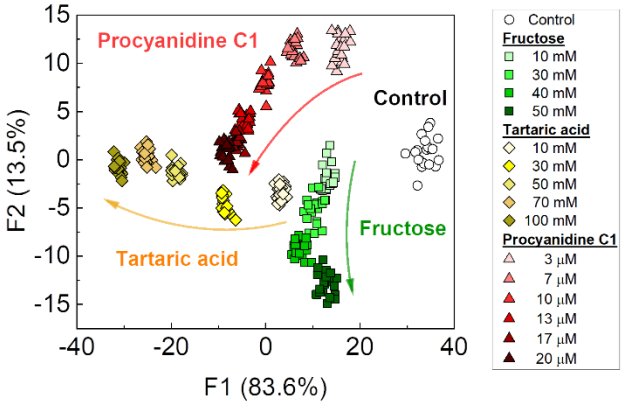


On-site Detection Optical Devices

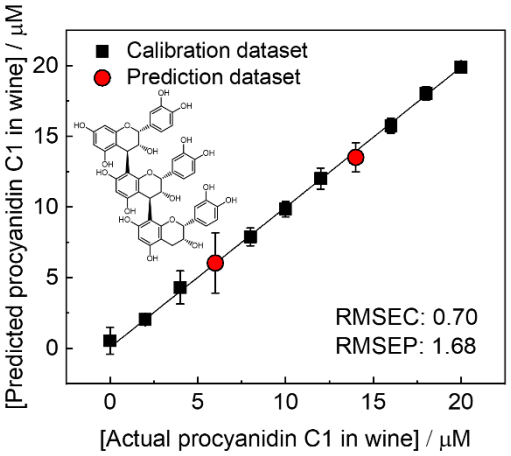
Quantitative discrimination on glass chips by imaging analysis



Semi-quantitative assay



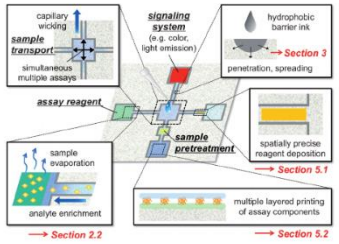
Regression analysis in a wine



T. Minami et al., *Chem. Eur. J*. **2020**, *26*, 16236. (Cover)

Paper-based analytical devices (PADs)

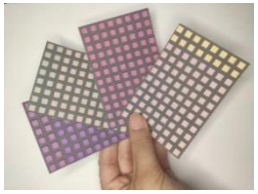
- Inexpensive, lightweight, and easy-to-store
- Requiring only small volumes of samples



G. M. Whitesides et al., *Anal. Chem.* **2009**, *81*, 5990.

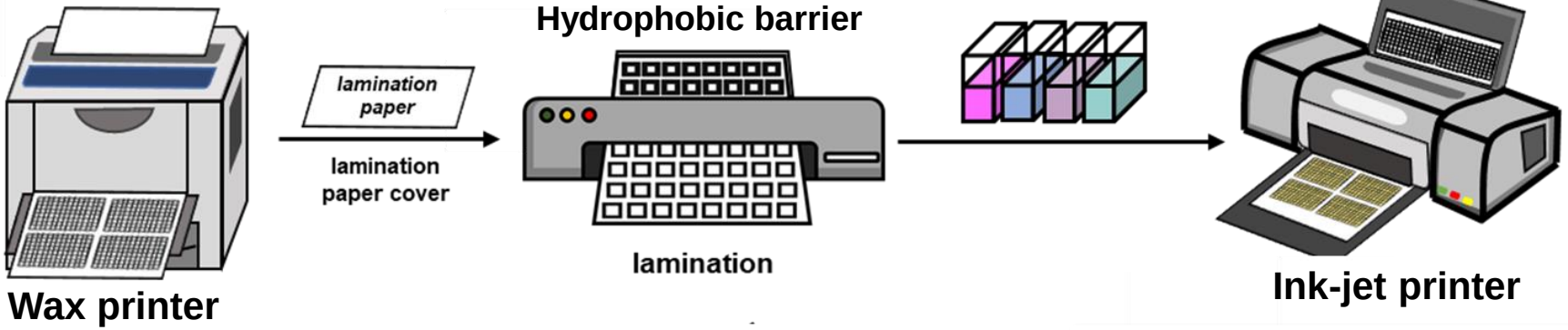
D. Citterio et al., *Angew. Chem. Int. Ed*. **2015**, *54*, 5294.

Aim: **Development of paper-based "chemosensor array" device (PCSAD) for quantitative assay**

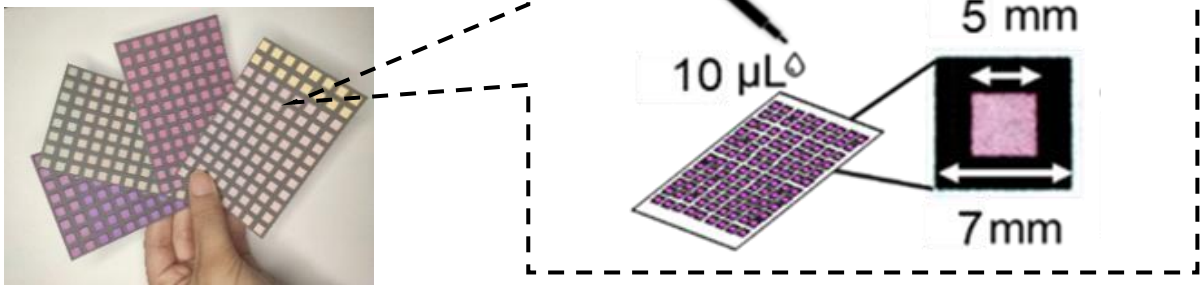


A Paper-based Array

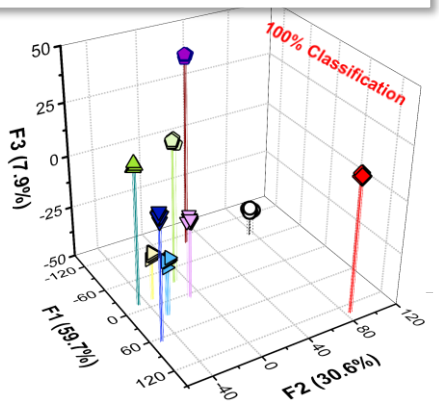
Fabrication process



Target detection



Discrimination of "species"



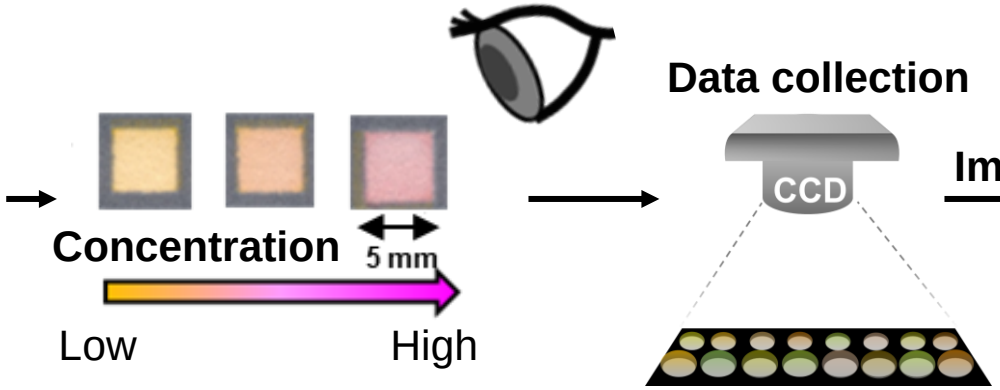
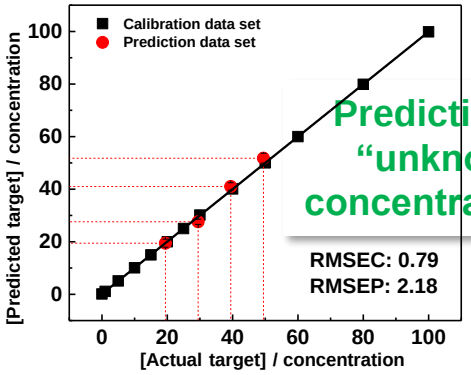


Image analysis



Prediction of "unknown concentrations"

T. Minami et al., *Anal. Chem.* **2021**, *93*, 1179.

International Collaborative Research Project

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Development of materials for RNA detection

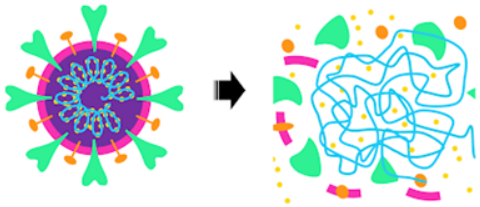
Collaboration

Minami group (Japan)

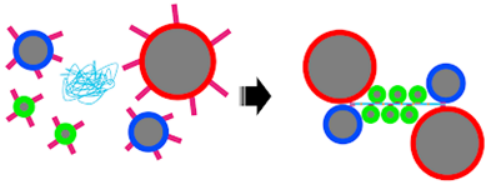
Establishment of paper-based array and image analysis

FindCov

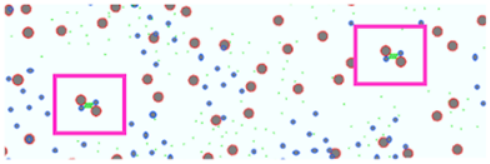
WP1: **Sample Processing**



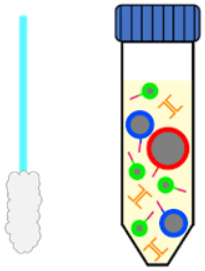
WP2: **Bead clustering on viral RNA**



WP3: **Clustering detection**



WP4: **Full Packaged-assay**

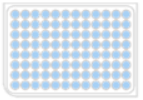


WP5: **Clinical Validation**

Simplicity

- Common equipment
- Ship by post *(no enzymes)*

High Speed



96 tests in **1h**

Low cost

1 test < **1€**