資料1-1
科学技術・学術審議会 研究計画・評価分科会
第9期ナノテクノロジー・材料科学技術委員会
ナノテクノロジー・材料分野の研究開発戦略検討作業部会
（第5回）

YASKAWA

AIST
NATIONAL INSTITUTE OF
ADVANCED INDUSTRIAL SCIENCE
AND TECHNOLOGY (AIST)

RBI

Robotic Crowd Biology with Maholo LabDroids

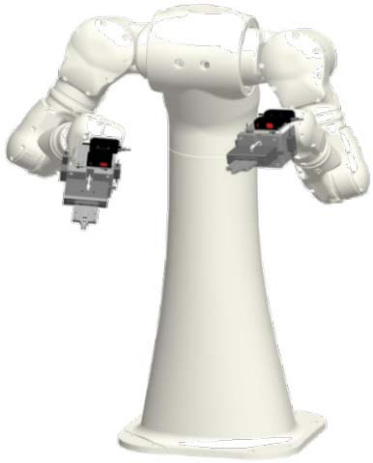
Tohru Natsume, Ph.D.

Molecular Profiling Research Center for Drug Discovery
Research Director

Robotic Biology Institute Inc.
Chief Scientific Officer (CSO)

Humanoid

A type of robot replicates or imitates human's skilled movement and maneuvers using same tools and equipment.



What the HUMANOID is NOT is ...
a dedicated automation machine.

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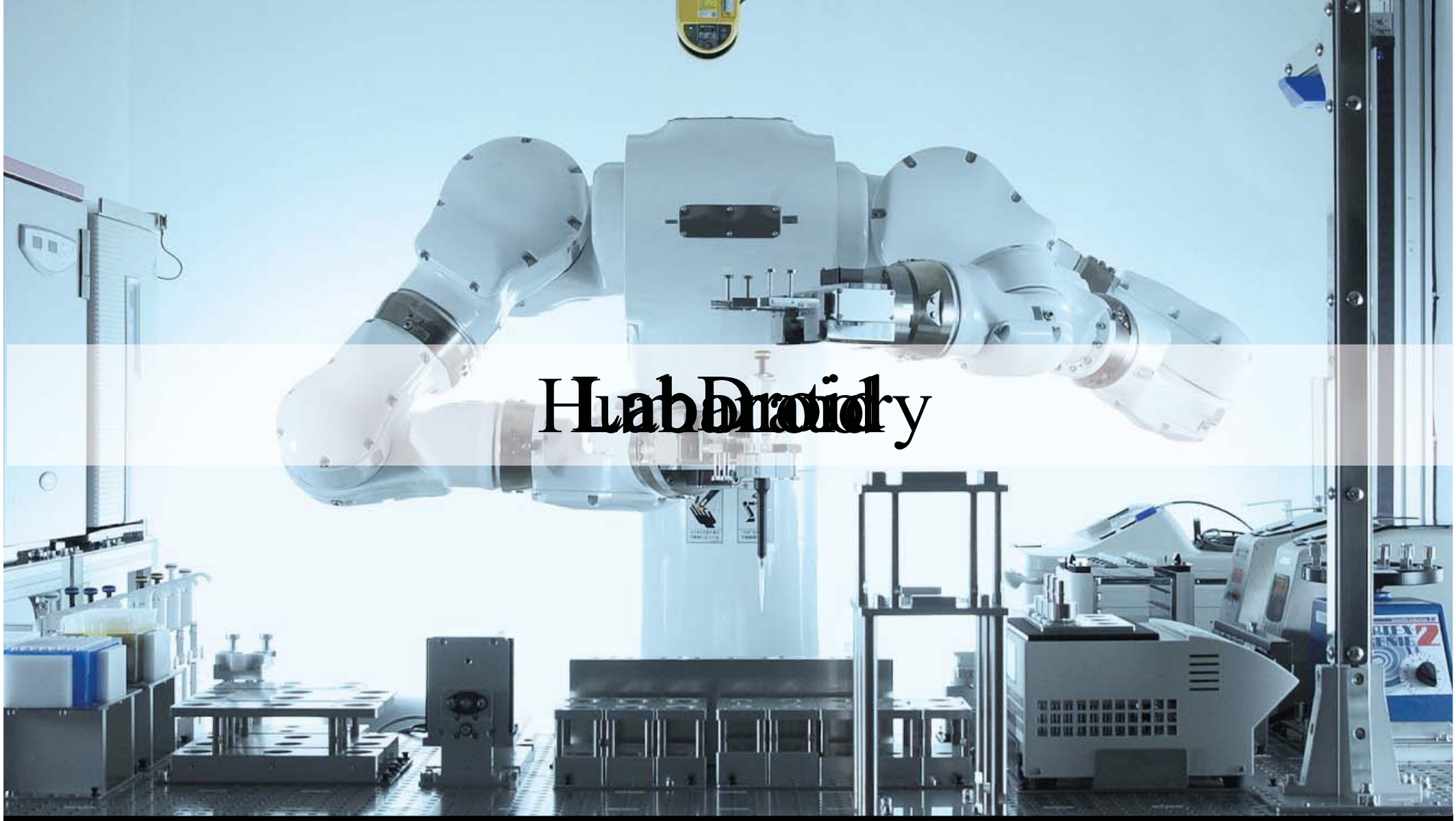


HuboDroid

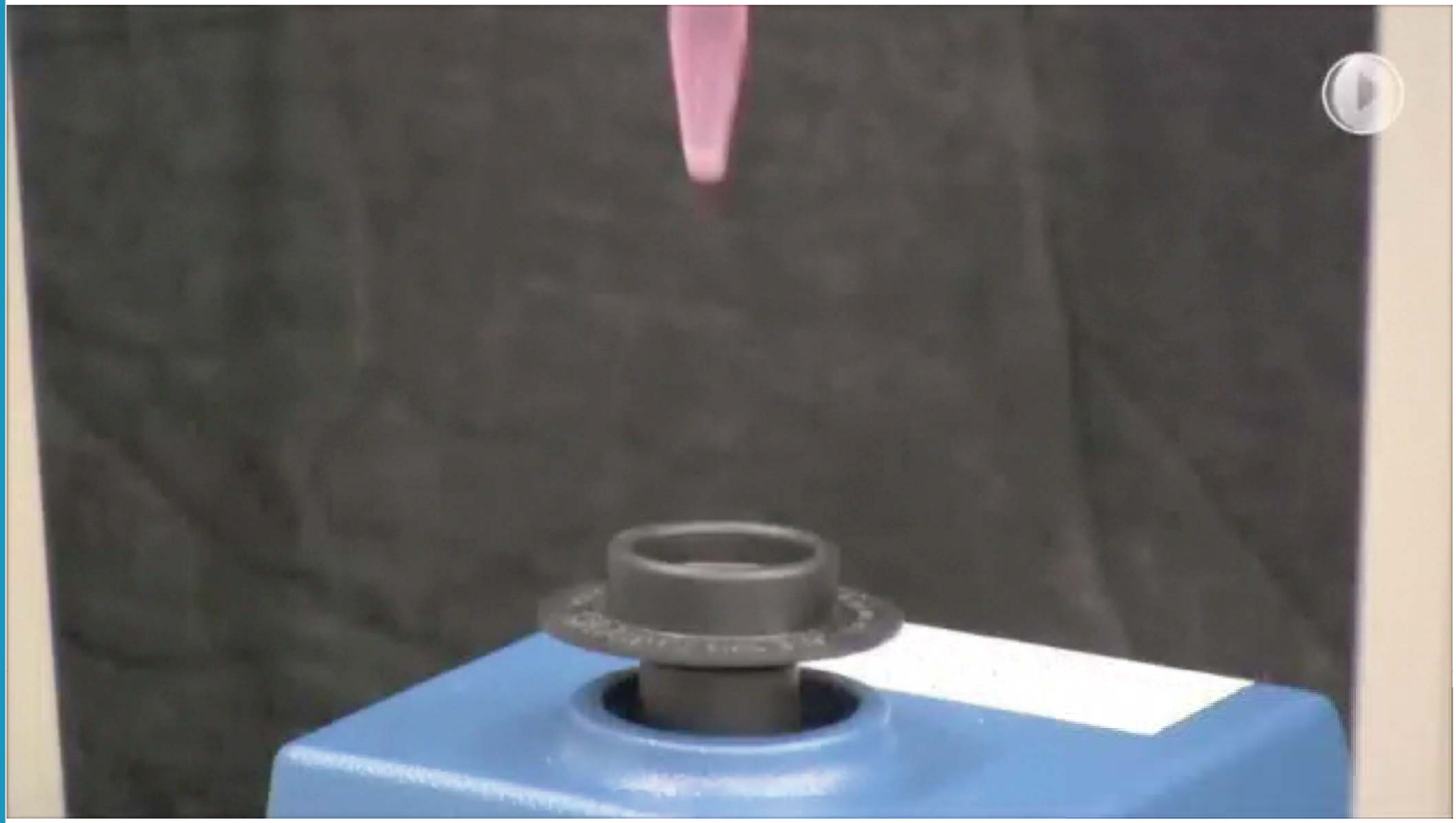
Researcher demand-oriented

Multi-operationality and expandability

Spin column manipulation

TCA protein precipitation

Vortex mixer



Cell Scraping

Jig free system

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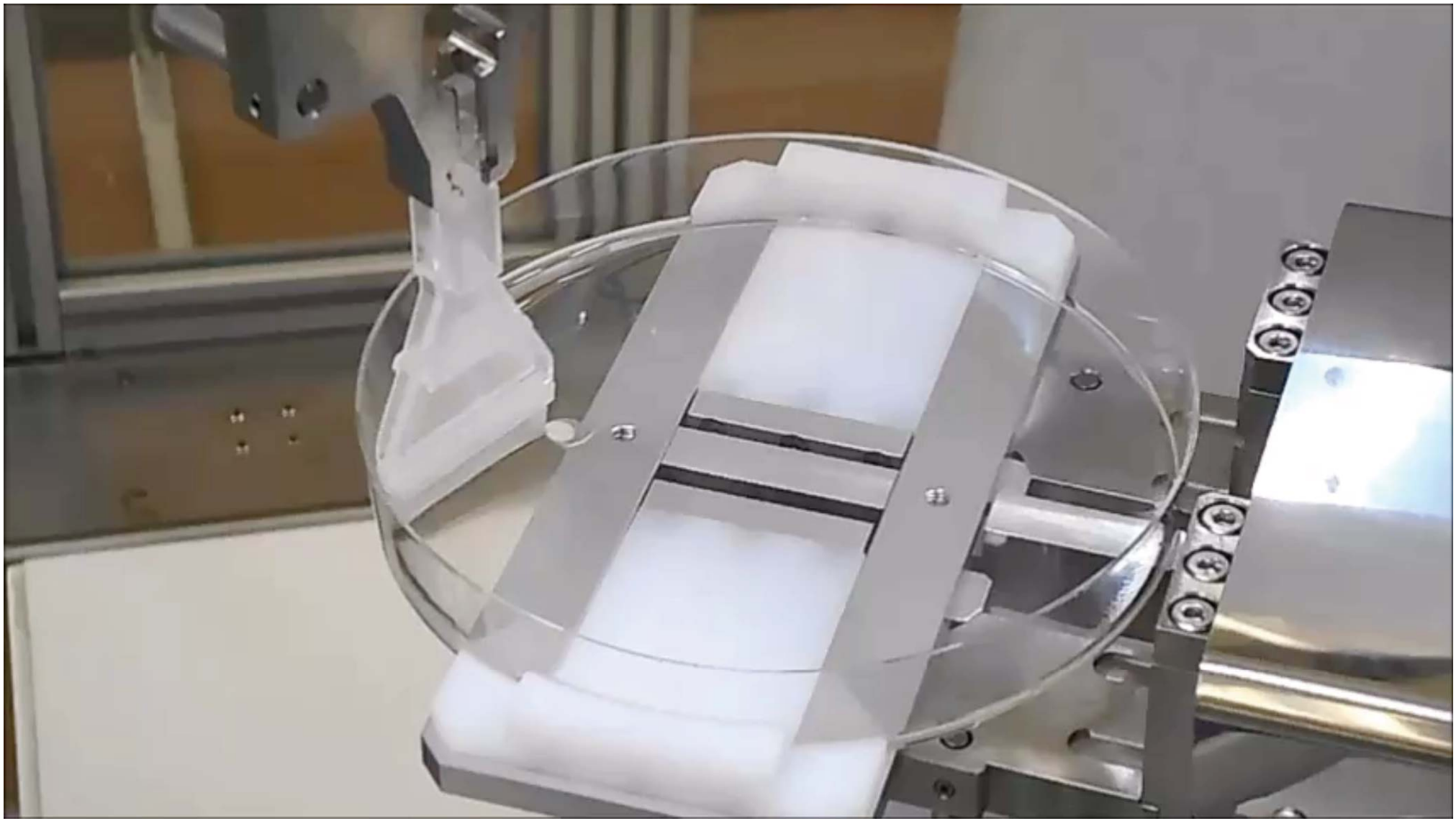
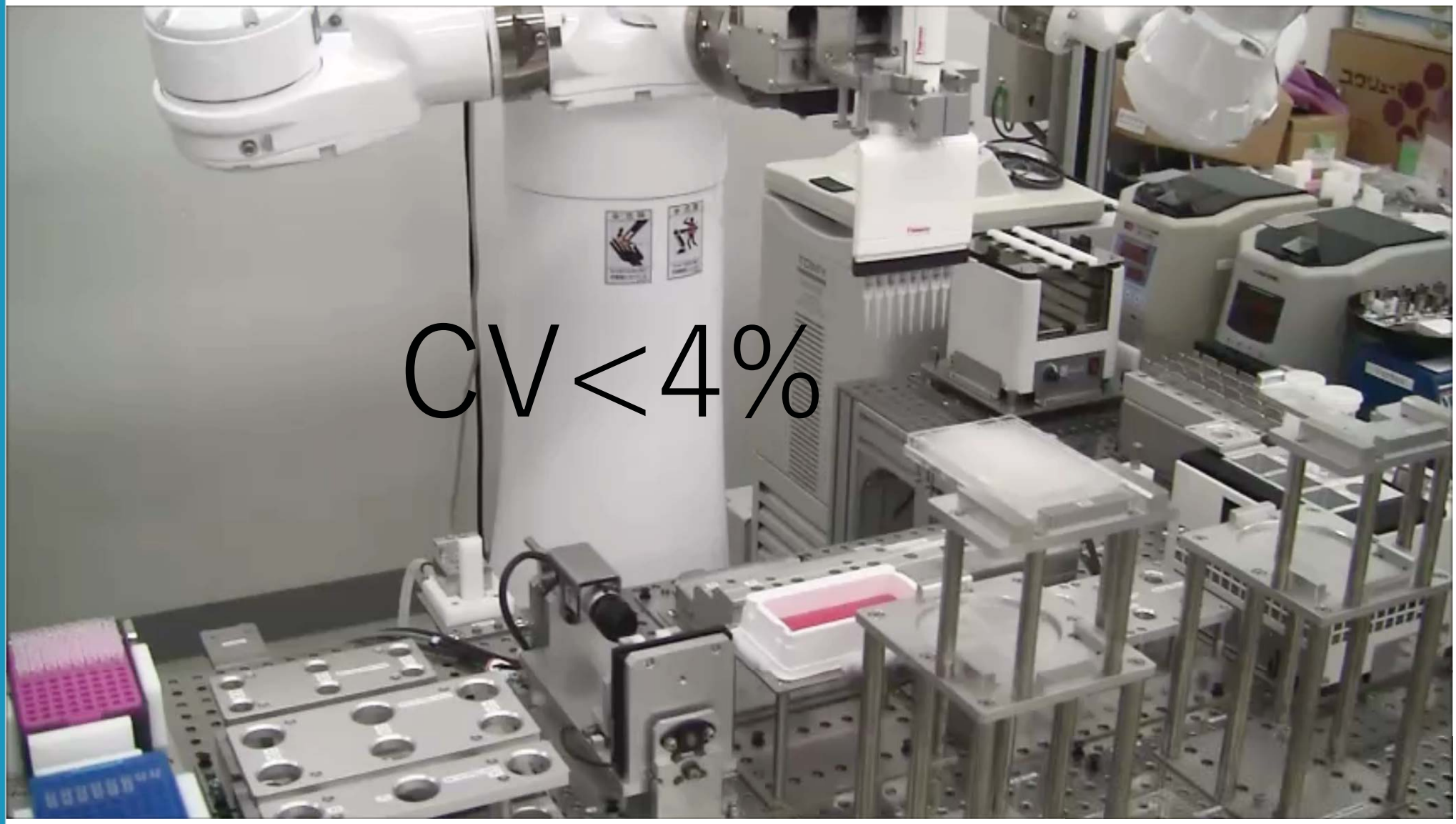
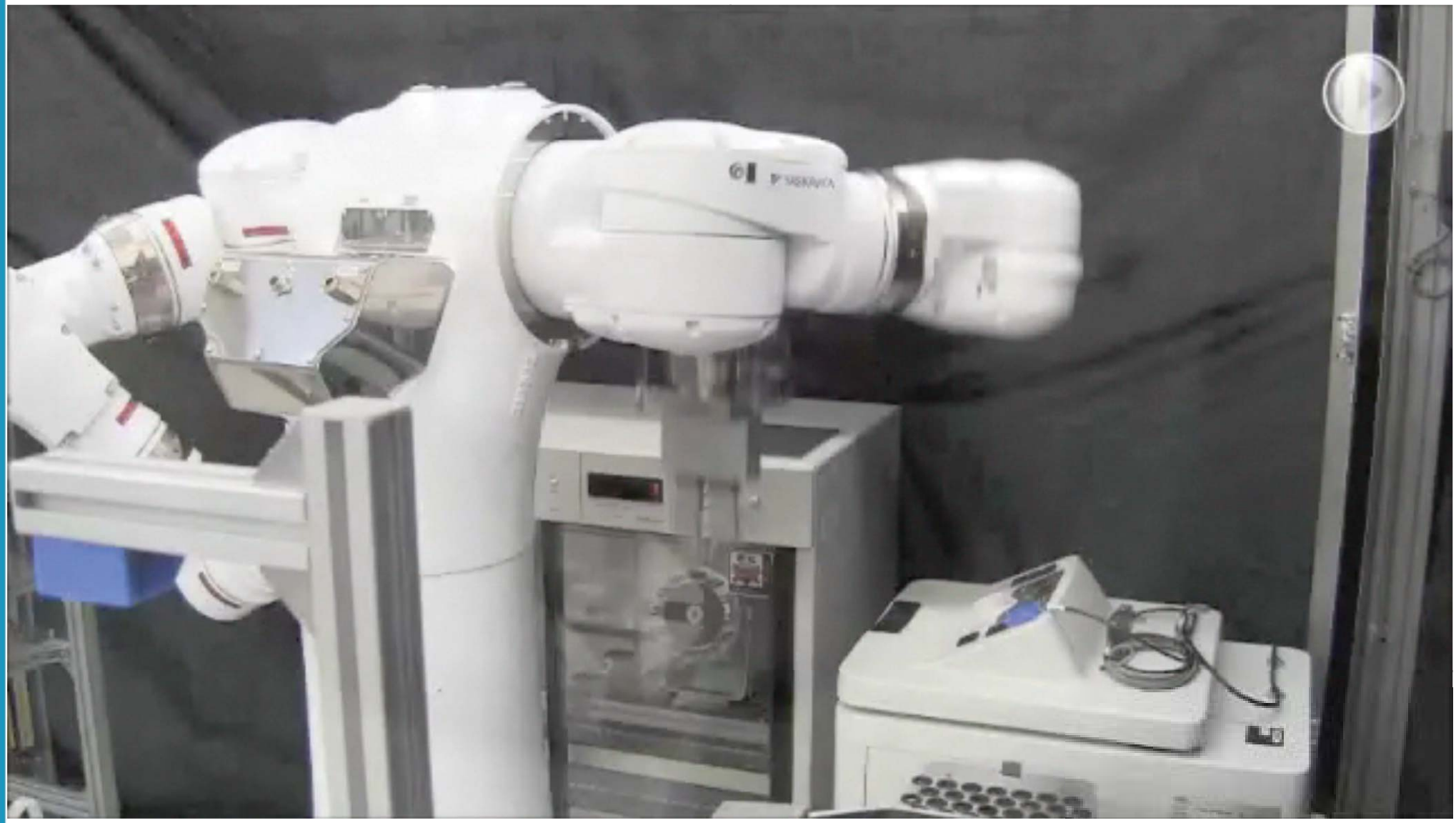


384 multiwell dispensing

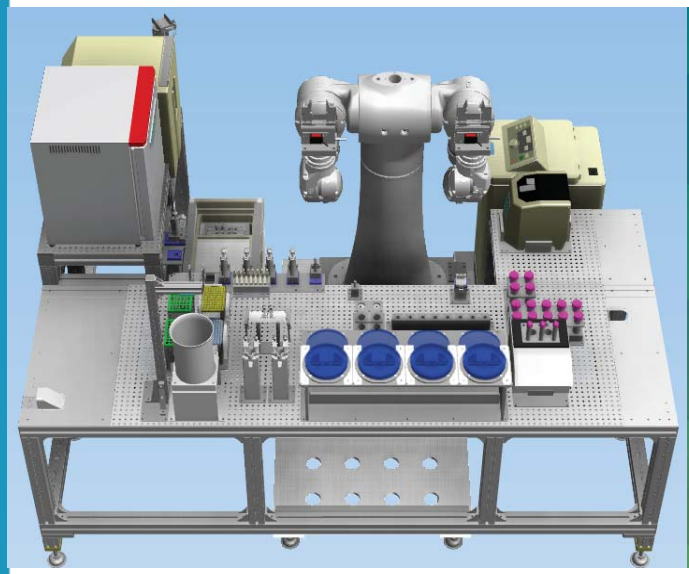


Fridge and Rotator

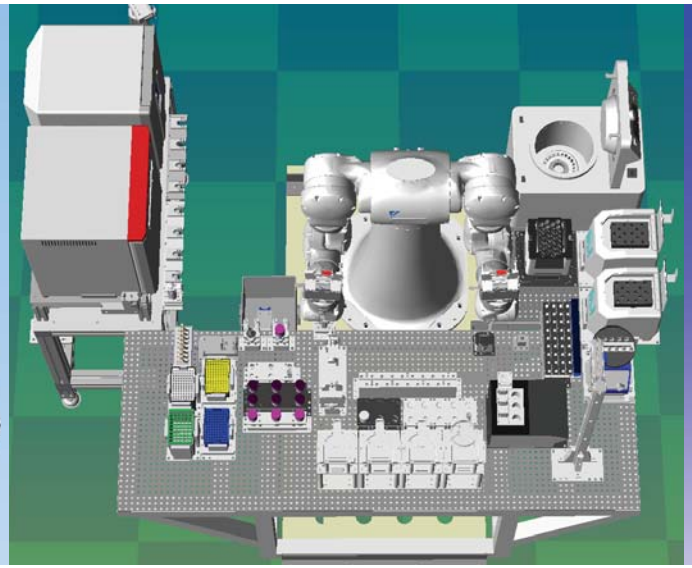


Versatility of LabDroid

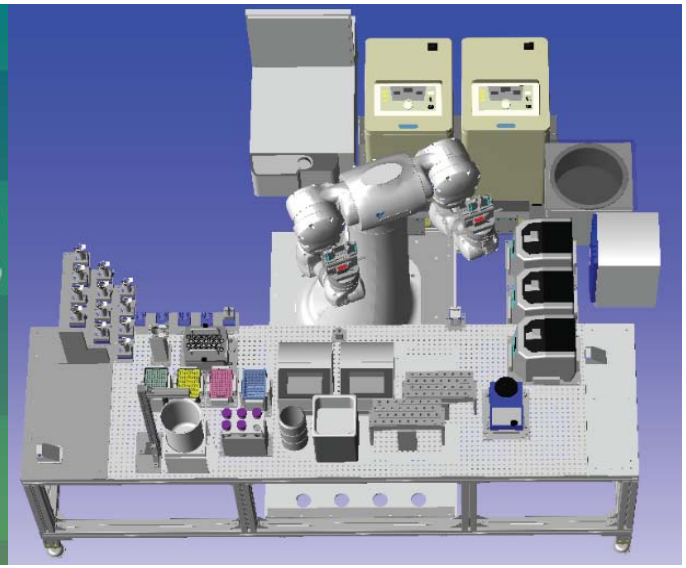
For Cell culture
Cell-based screening



For Proteomics
Metabolomics



For Genomics



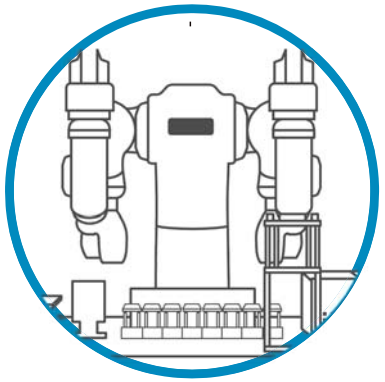
Beyond mere laboratory automation

LabDroid's main value: Optimization and standardi[illegible] of protocols

Improve efficiency and cut costs

Transfer human skills and expertise/maneuverability to LabDroid

Visualize and digitize human skills and expertise/tacit knowledge



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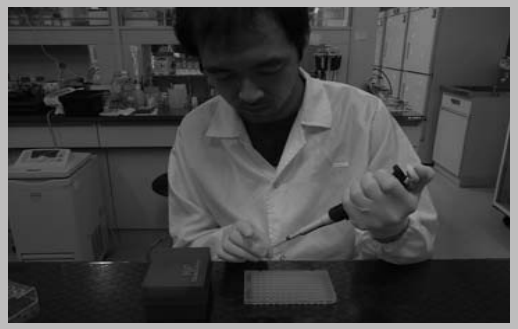
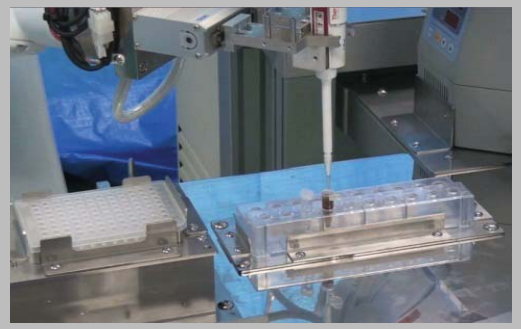
Ex. 1 | Reproductibility in real-time PCR

Microvolume dispensing – accuracy crucial for quality results

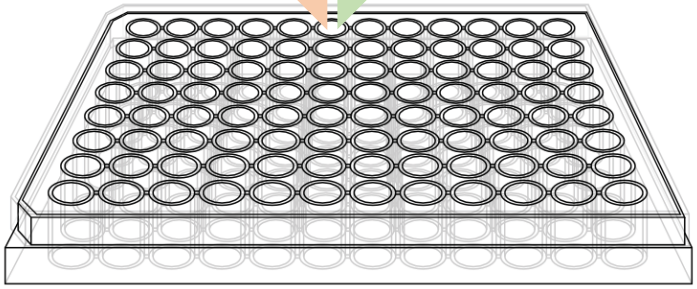


VS



cDNA, Primers

Enzymes, dNTPs, Buffer



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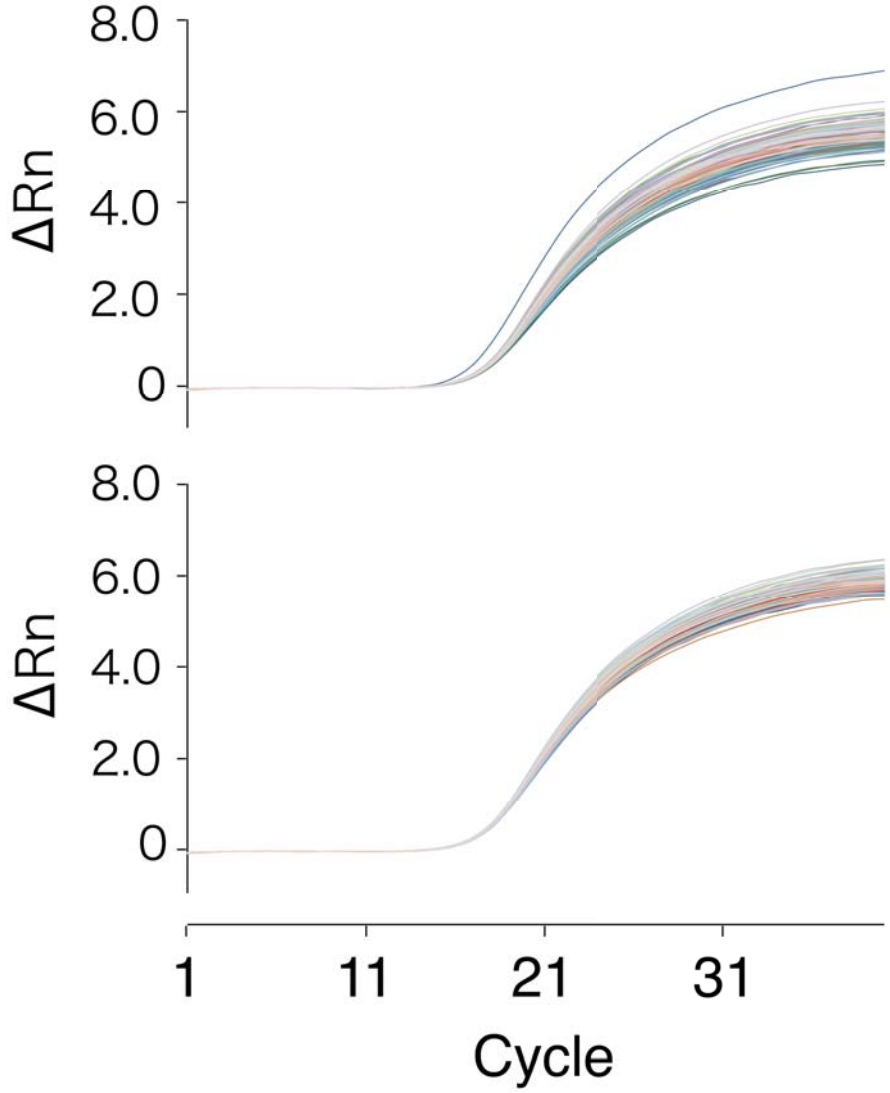
LabDroid outperforms skillful humans

Real-time PCR profile



Manual

CV ~ 10-20%

LabDroid

CV < 4%

Record-breaking performance

RBI

LabDroid outperforms skilled humans

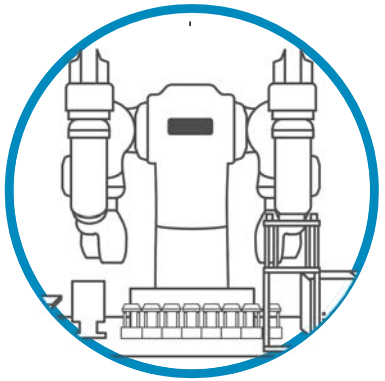
Real-time PCR competition: humans *vs* LabDroid

Best performer

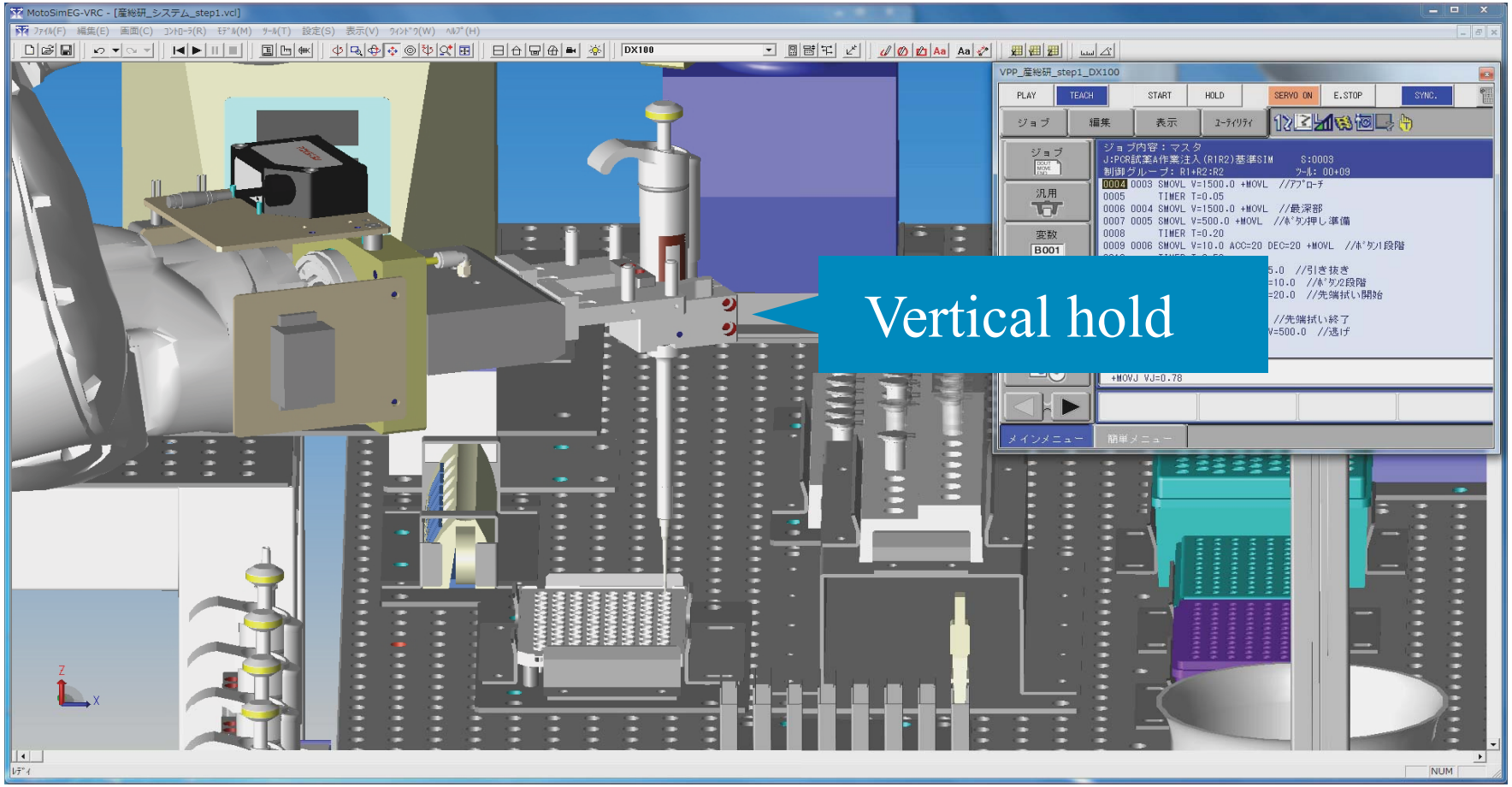
CV = 10%

LabDroid

CV < 4%



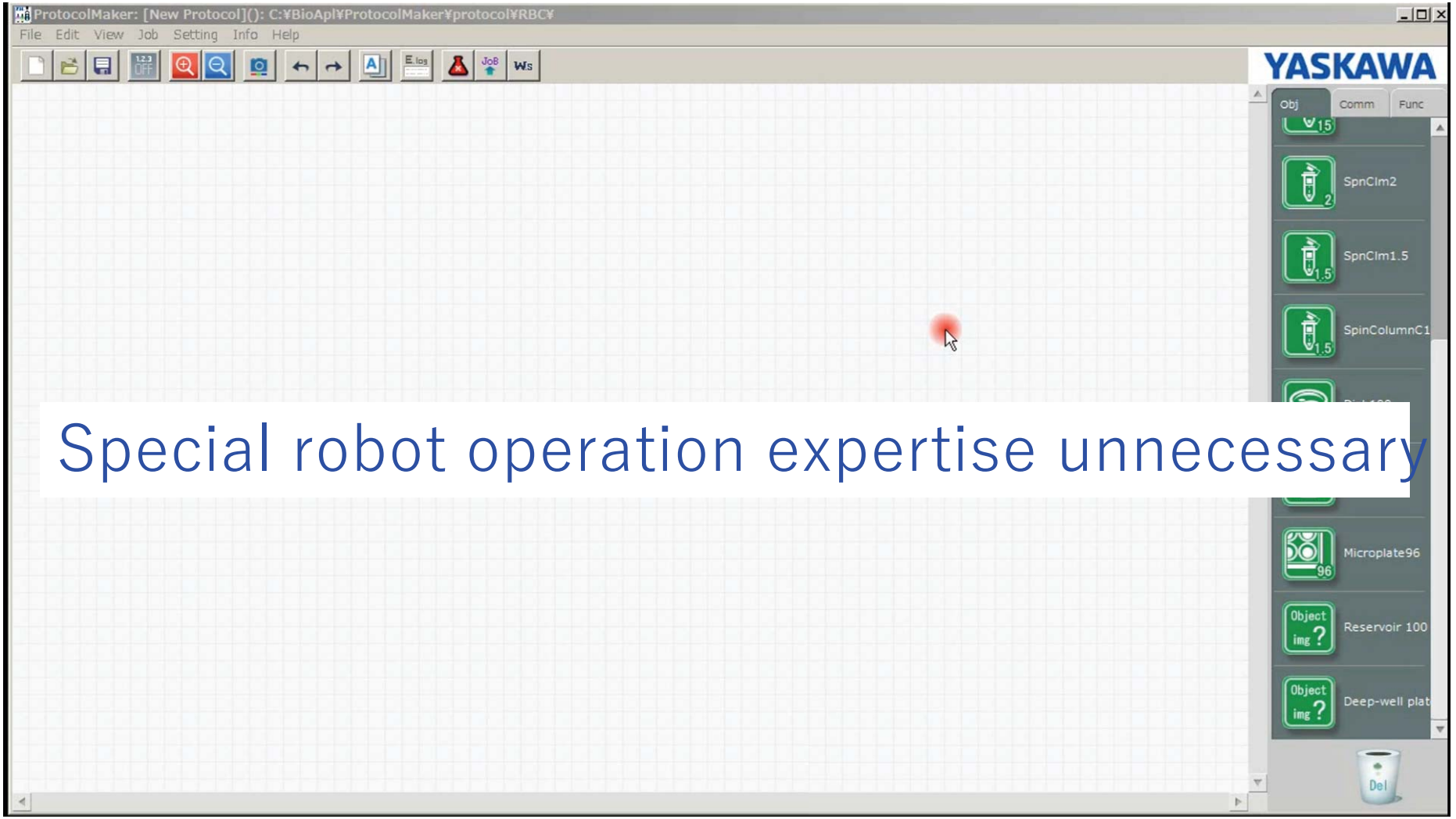
Optimize performance of µL scale pipetting



Step 1 | Tip down 2 mm above well bottom
2 | First plunger push at 15 mm/sec
3 | Move tip up 2 mm, 0.5 mm/sec
4 | Wait 0.5 sec
5 | Second plunger push 30 mm/sec
6 | Raise
7 | Move up vertical

Optimization interface: Protocol Maker

LabDroid is operated from a PC or tablet, equipped with software that allows researchers to set up any protocol simply and intuitively.



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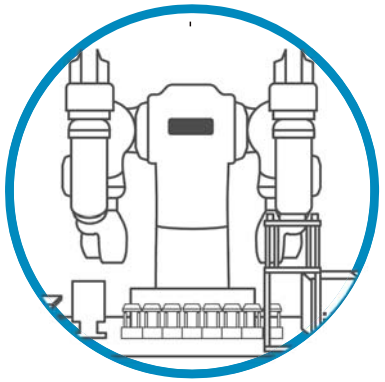

Ex. 3 | Cell-based high-content screening

Failed to narrow down chemical library to discover hit chemicals by humans. Two researchers struggled for 2 years.

LabDroid achieved successful results on the first attempt!

Keio University School of Medicine

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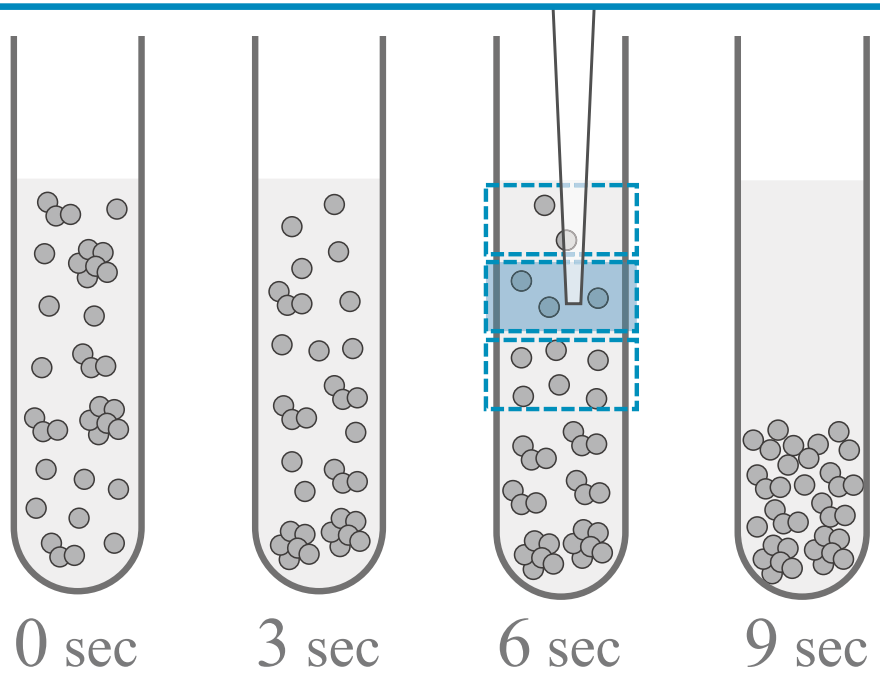
Why do LabDroids succeed?

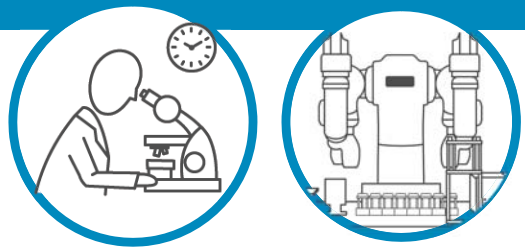
Reasons for difficulty: Two conflicting factors

Cells must be separated into single cells and then inoculated in each well evenly	Pipetting into single cell completely damaged cells

Retrieve only from particular depth where cells are dispersed equally with optimum density

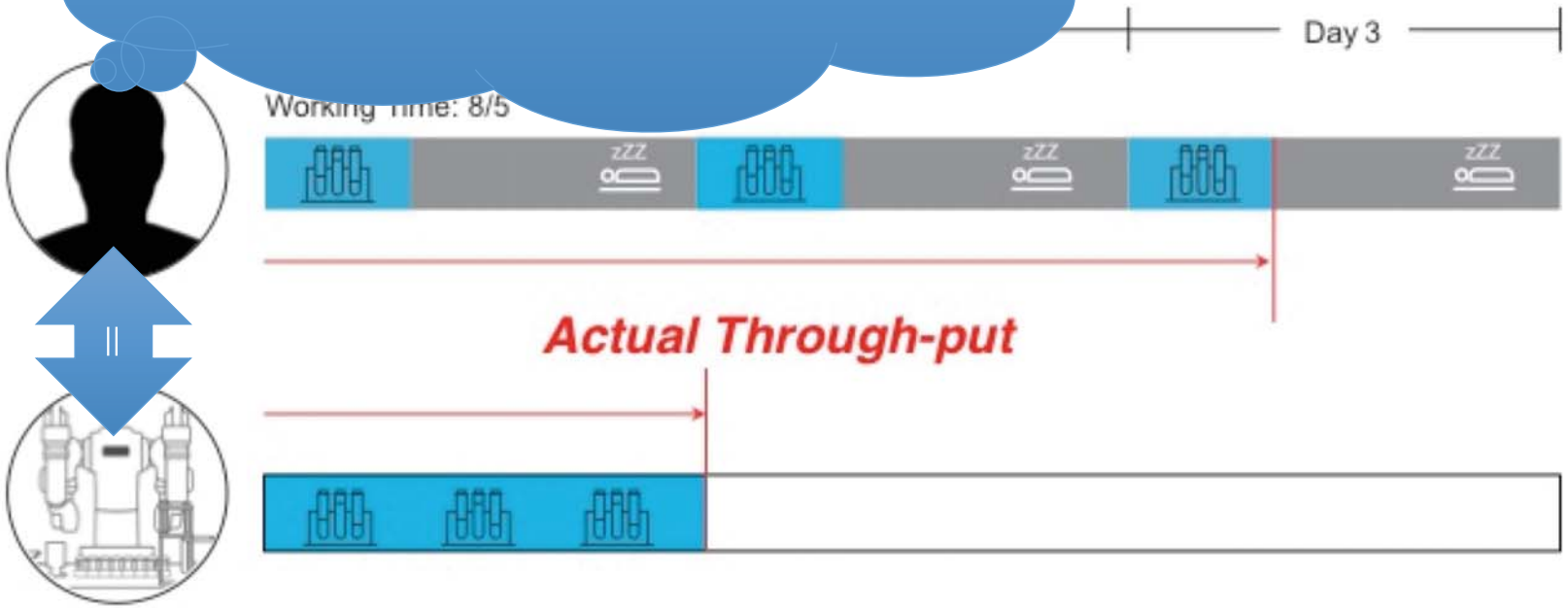


Items optimized
1) Dispersion Intensity (viability > 90%)
2) Depression time
3) Tip position



LabDroid-Researcher collaboration found condition in just one week!

ChIP protocol = 17hrs
Humans can not complete the workflows
in a normal 8-hour work day



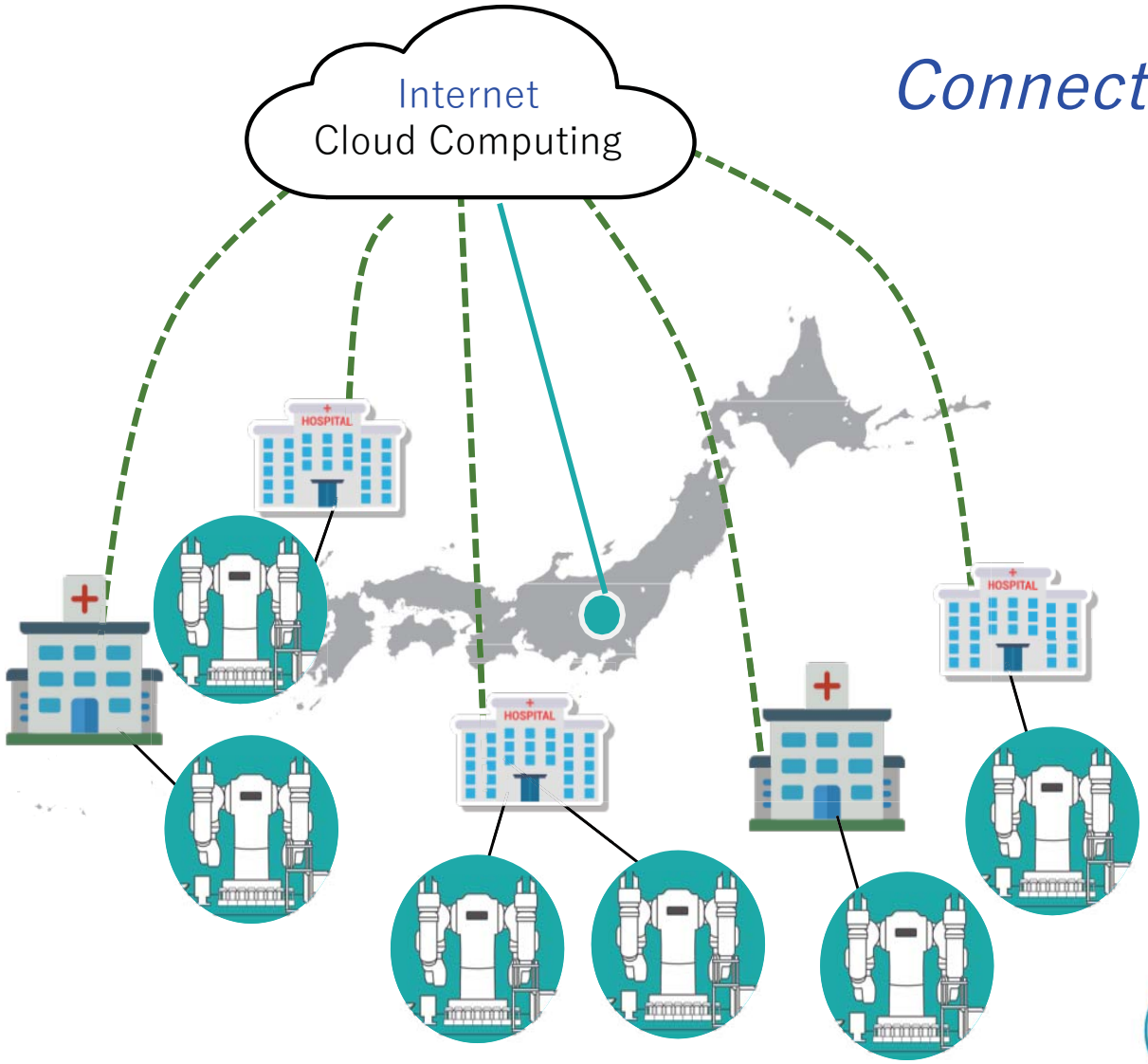
Automation of life science

past, present, and future

Automation of life science

past, present, and future

16 LabDroids are already hard at work in JAPAN



Connecting Robots!

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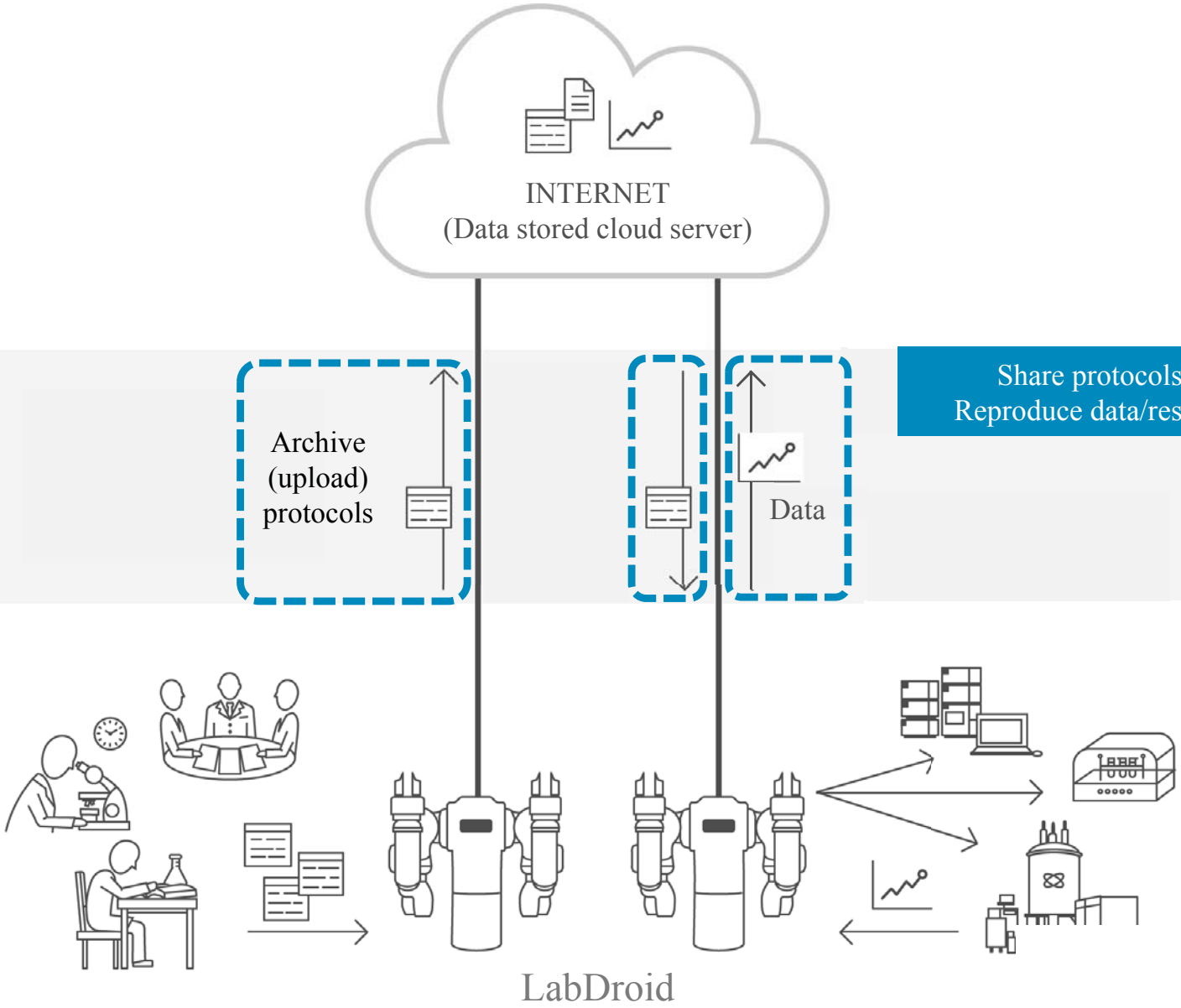
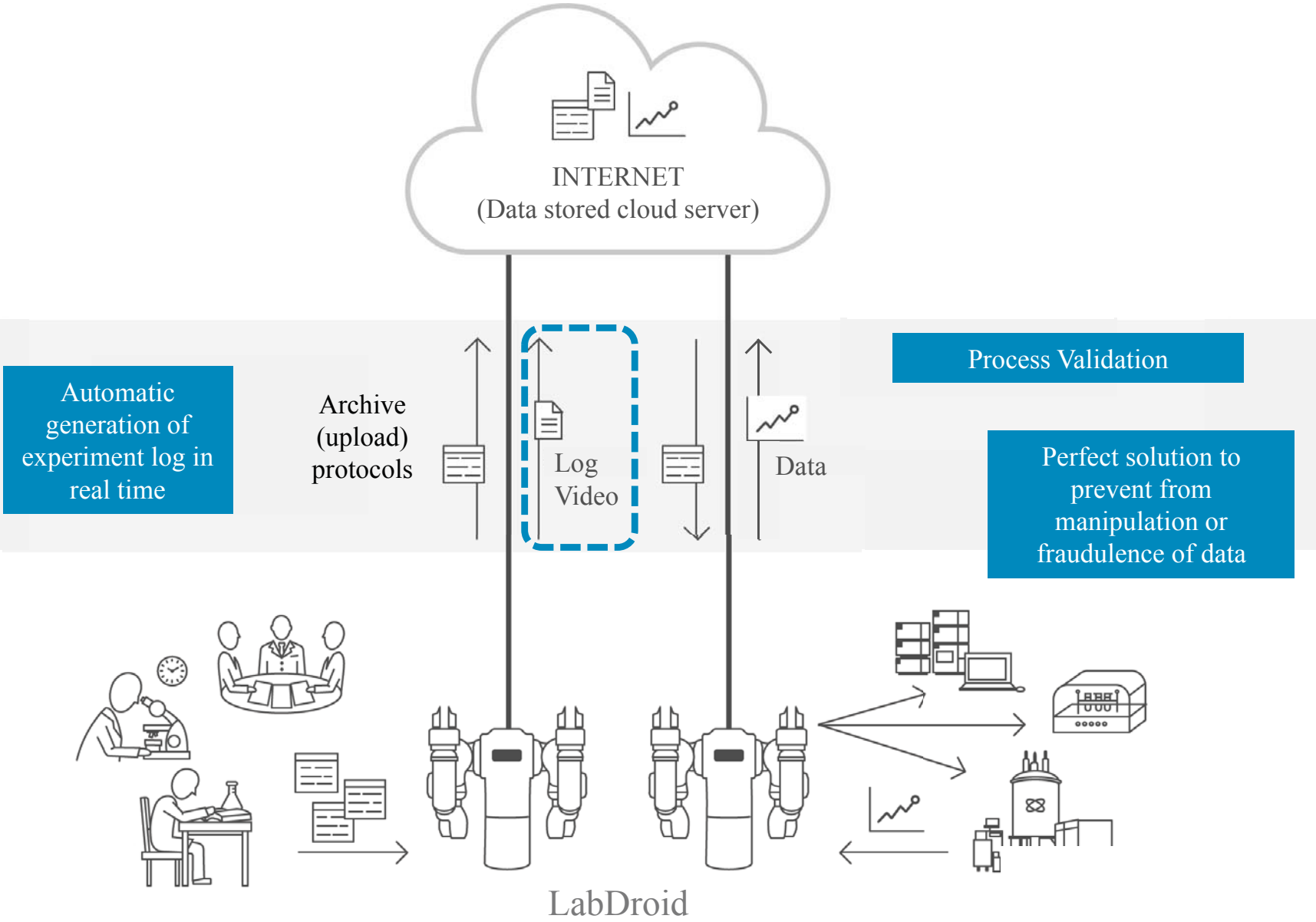
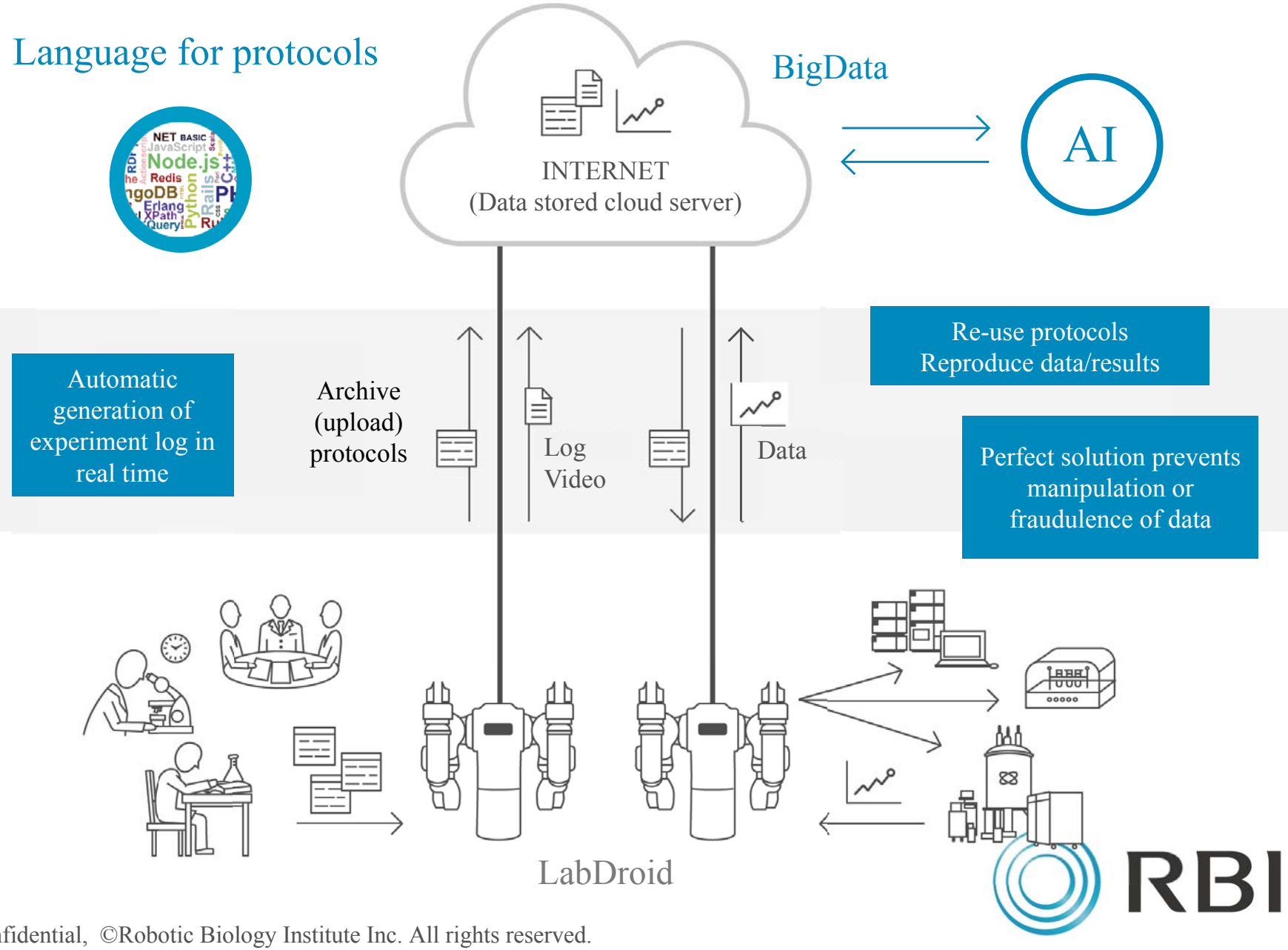
Total laboratory management system



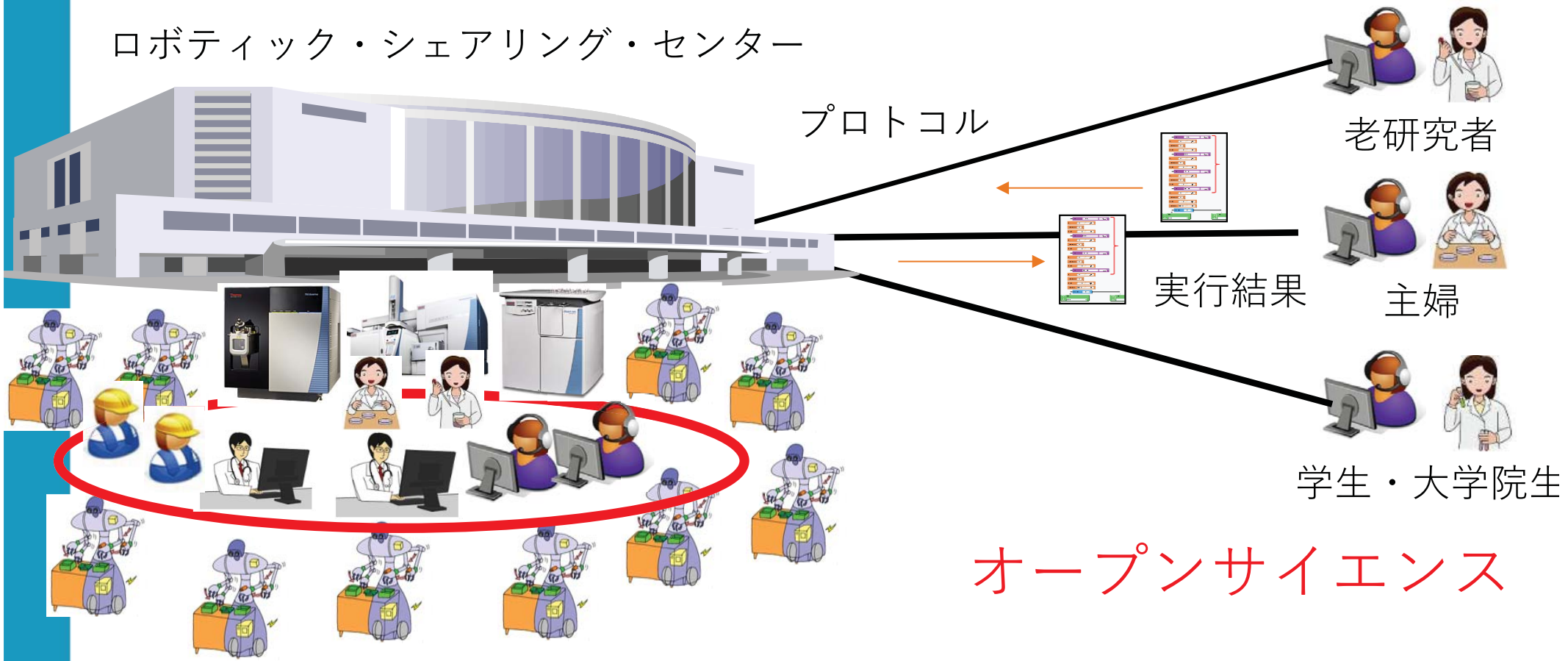
Total Laboratory Management System



LabSphere : Laboratory on Cloud



働き方の未来：在宅研究の促進



オープンサイエンス

徹底的な人材活用

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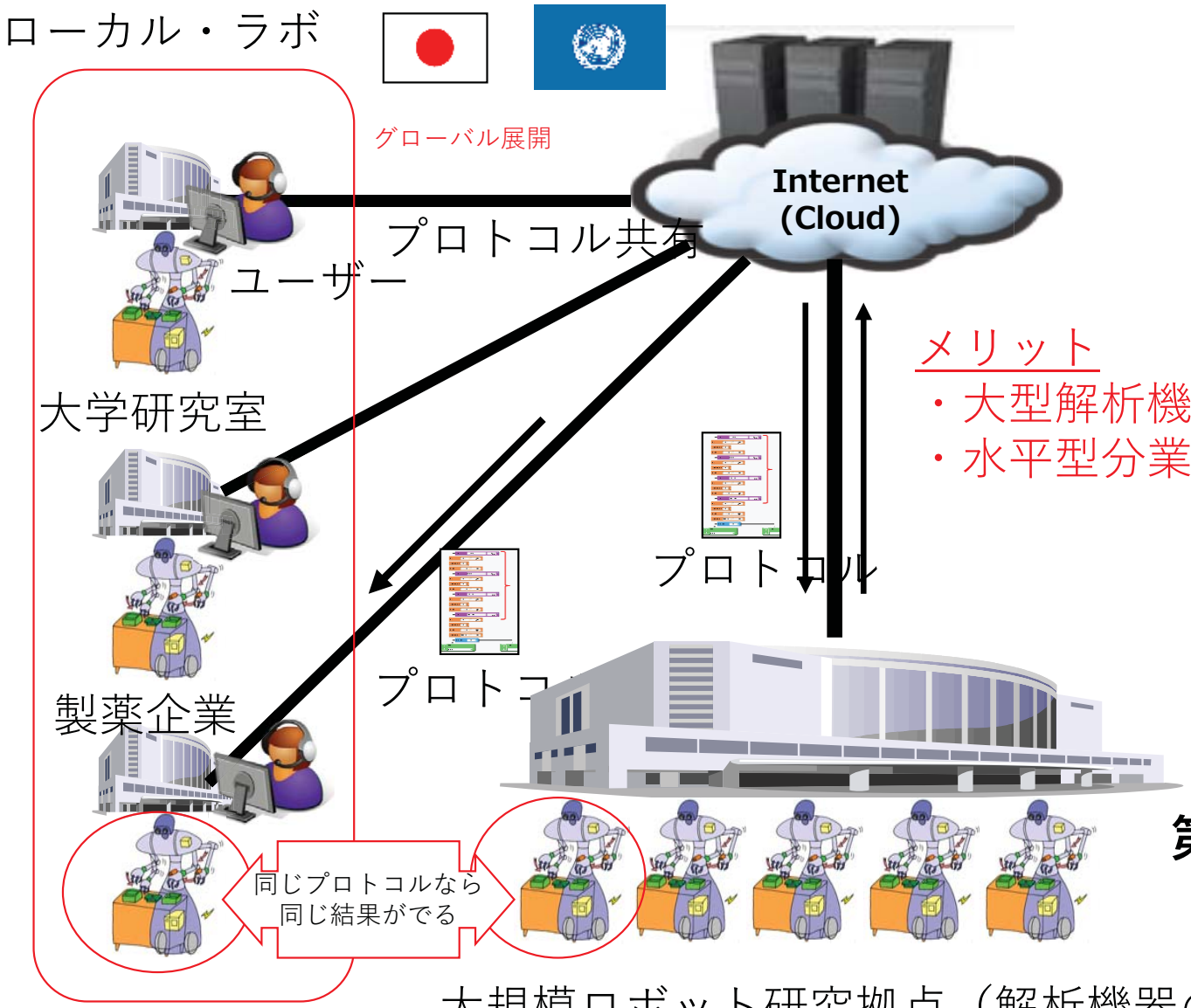
次の未来：クラウドで繋がっていく
～大規模ロボット研究拠点の創成



メリット
- 大型解析機器の稼働率アップ
- 水平型分業・研究拠点の差別化

第三者認証が可能

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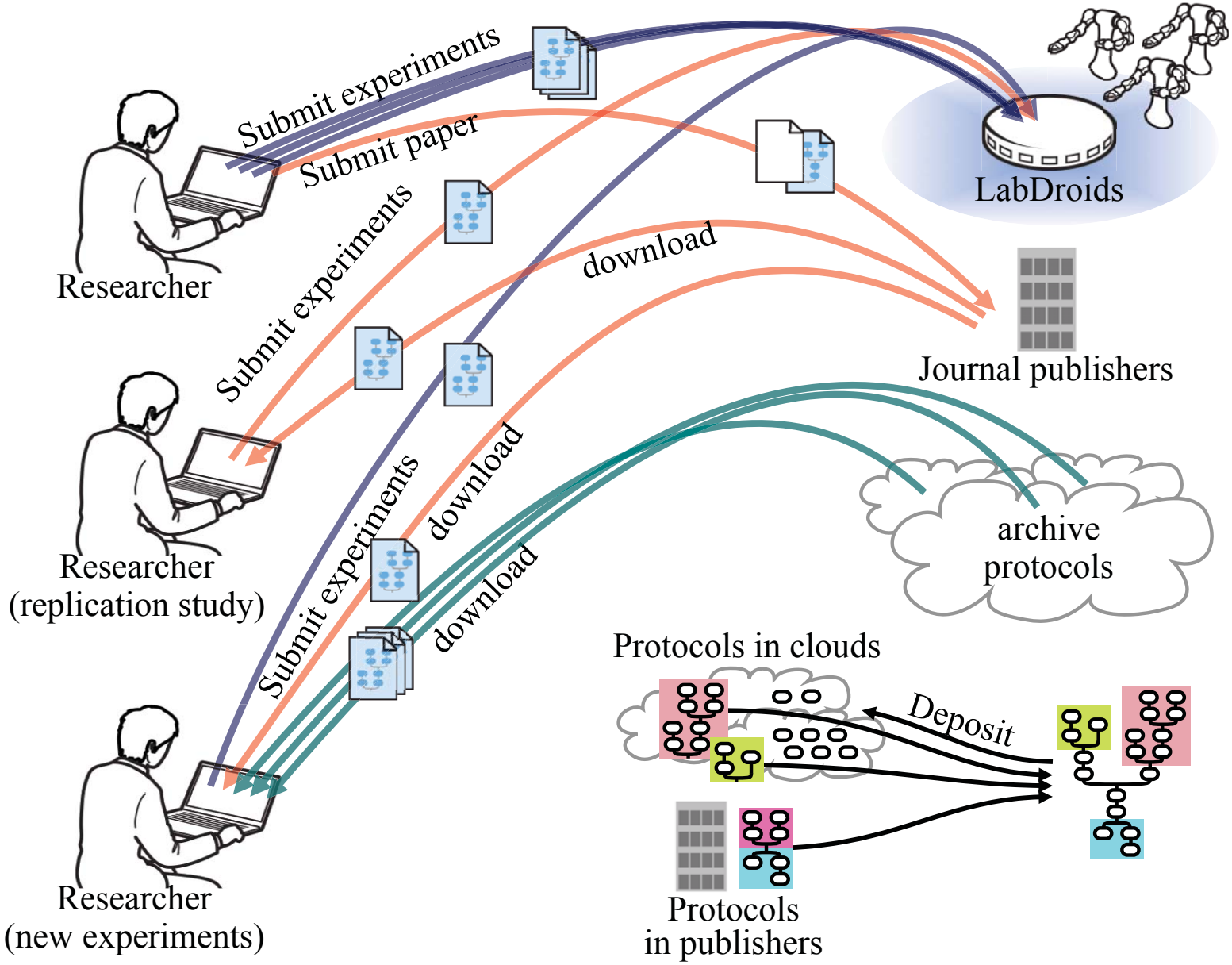
Collaboration through LabSphere



N Yachie, T Natsume. "Robotic crowd biology with Maholo LabDroids", *Nature Biotech*. 35, 310–312 (2017).

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■ライフサイエンス/バイオインダストリーの抱える問題

研究生産性の低さと再現性

研究・実験が再現しない理由
技術と経験が、暗黙知として個人に囲い込まれているため、再利用・共有が不可能。
実験の成功は個人の技術・経験頼り、その上再現性が低い。

担当者が変ると、プロジェクトが頓挫する。前任者の技術基盤が、何も残らない。
人材確保が困難。研究開発の安定的継続の危機！

過去5年間＝8.6兆円
今後２～３倍増加予測
新薬開発は産業として成り立たなくなる・・

結果：無駄な失敗、堂々巡り、試行錯誤を延々と繰り返す！
＝膨大なコストと時間
研究生産性が低い真因

スキル・経験の必要な最先端技術の導入が困難

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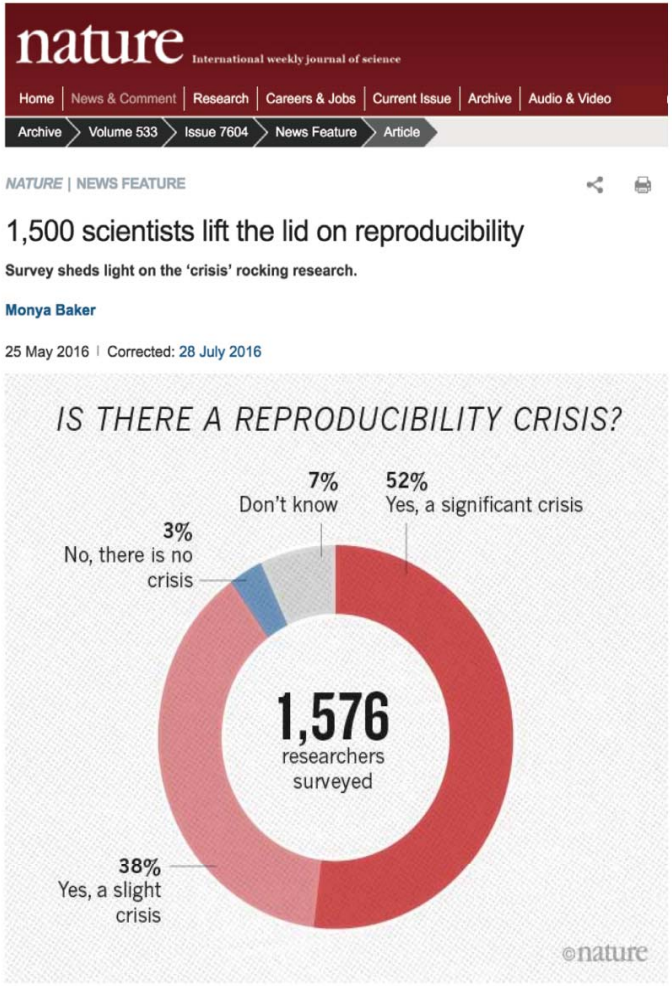
「再現性の危機」は問題点の根幹

Nature誌を初め、ライフサイエンス界では、「根源的な問題」として認識



(Baker M., Nature, **533**, 2016)

現在の生命科学の問題点

- 再現性
  - M Baker, Nature (2016)
    - 52% の人が「深刻な問題がある」と答えている
    - 70% の人が「実験の再現に失敗したことがある」
  - Iqbal SA et.al., Plos Biol. (2016)
    - 267/268 の論文の手法の記述が不十分
- 不正行為
- 労働集約的なワークスタイル

再現性は他の問題点の根幹である

- 再現性
  あるところで行った実験が、別のところででも再現するから、巨人の肩の上に立てる
- 不正行為
  簡単に（他人の）実験が再現できないから、不正行為をしてしまう
- 労働集約的なワークスタイル
  同じ作業を正確に何度も繰り返すことは、人間には難しい

RBI

MAHOLO

まほろ

RBI Robotic Biology Institute Inc.

YASKAWA

独立行政法人
科学技術振興機構
Japan Science and Technology Agency

産総研
国立研究開発法人 産業技術総合研究所
NATIONAL INSTITUTE OF
ADVANCED INDUSTRIAL SCIENCE AND TECHNOLOGY (AIST)

内閣府産学官連携功労賞／ロボット大賞受賞