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Miniaturization of a metabolomics and fluxomics sample preparation workflow

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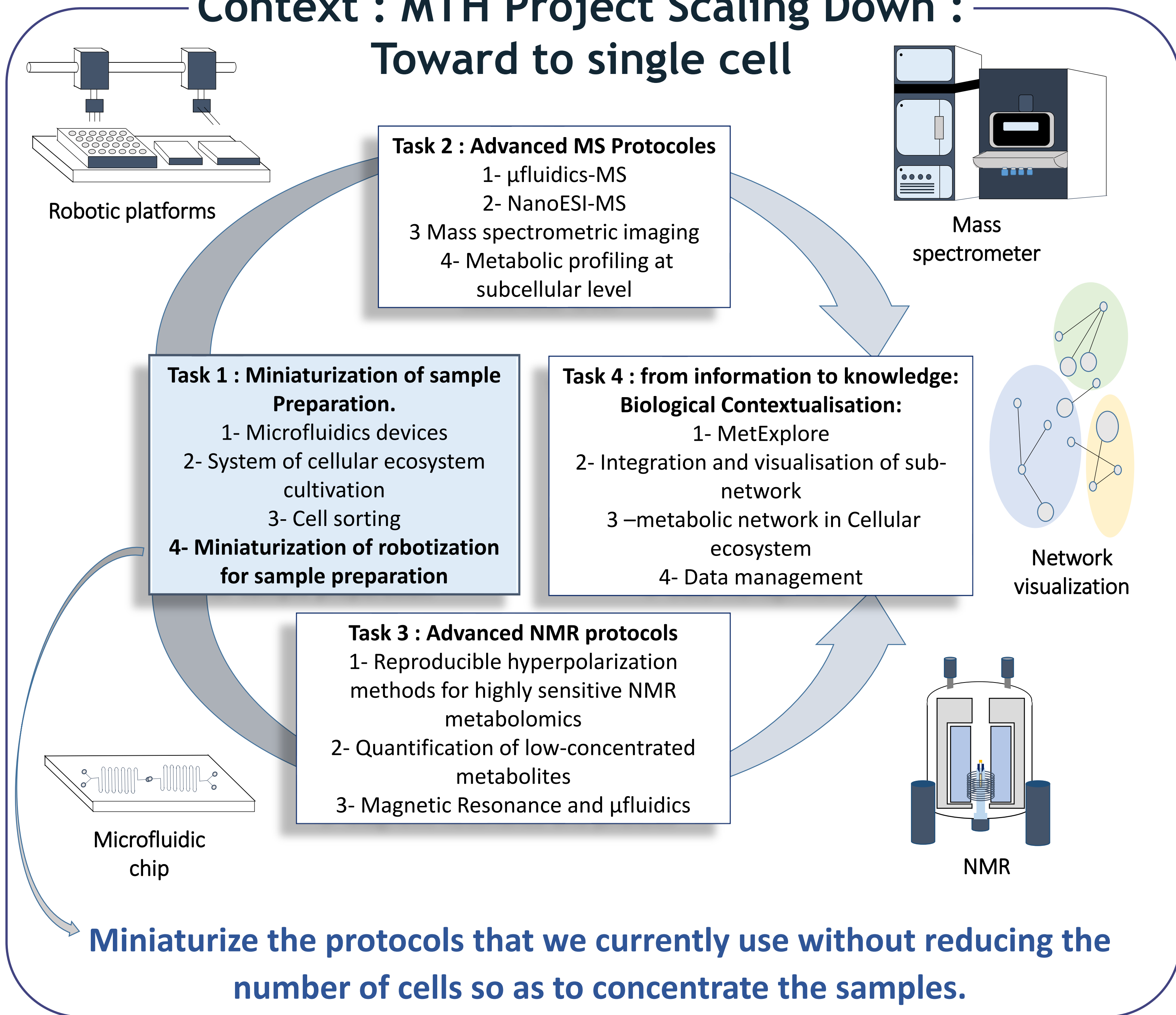
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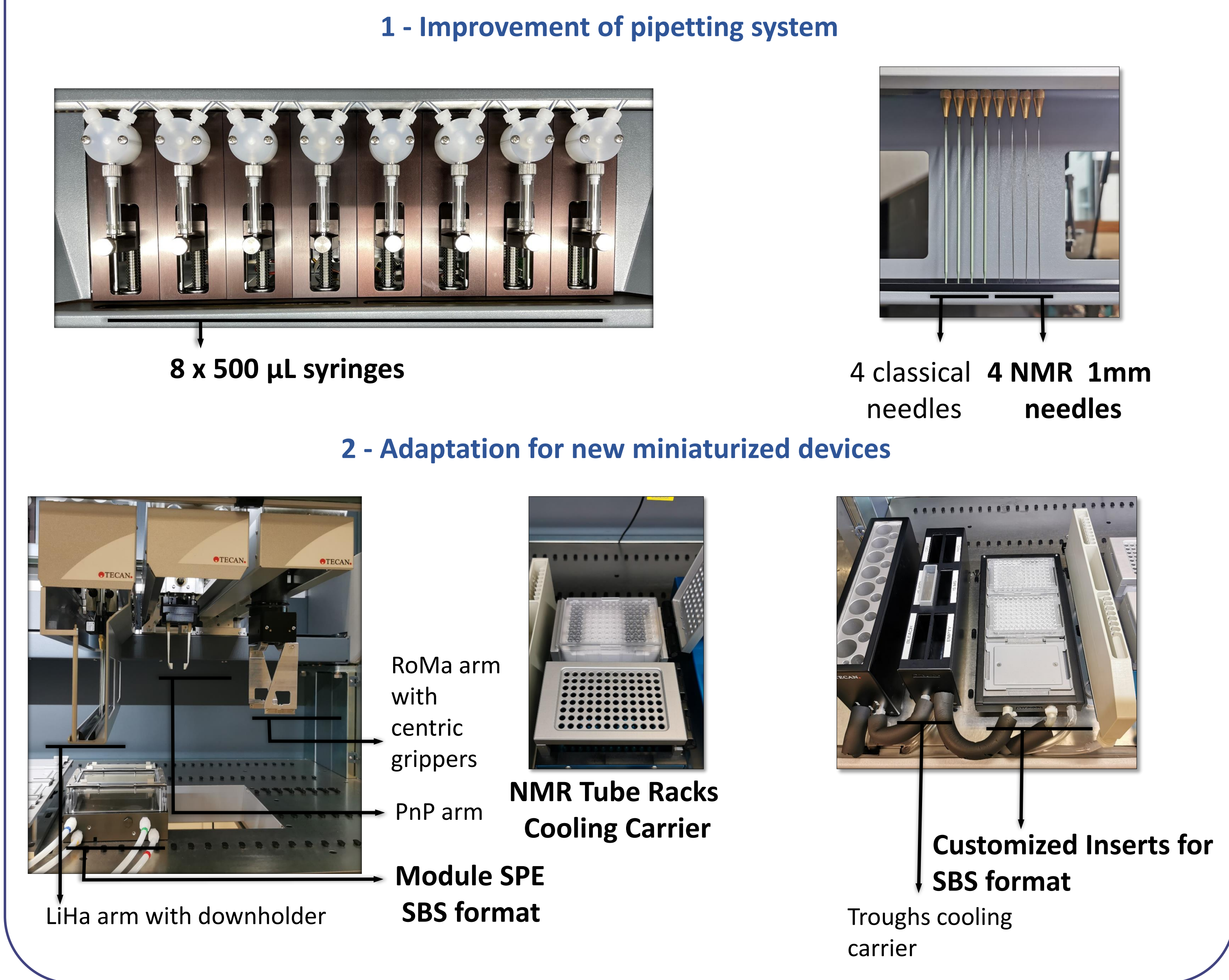
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² : MetaToul-MetaboHUB, National Infrastructure of Metabolomics & Fluxomics (ANR-11-INBS-0010)

Context : MTH Project Scaling Down : Toward to single cell



Robotic platform for miniaturized sample preparation



Results and discussion

1 - Improvement of pipetting of miniaturized volumes :

Development of a liquid handling robotic system suitable for pipetting 1 μ L with a CV < 10%

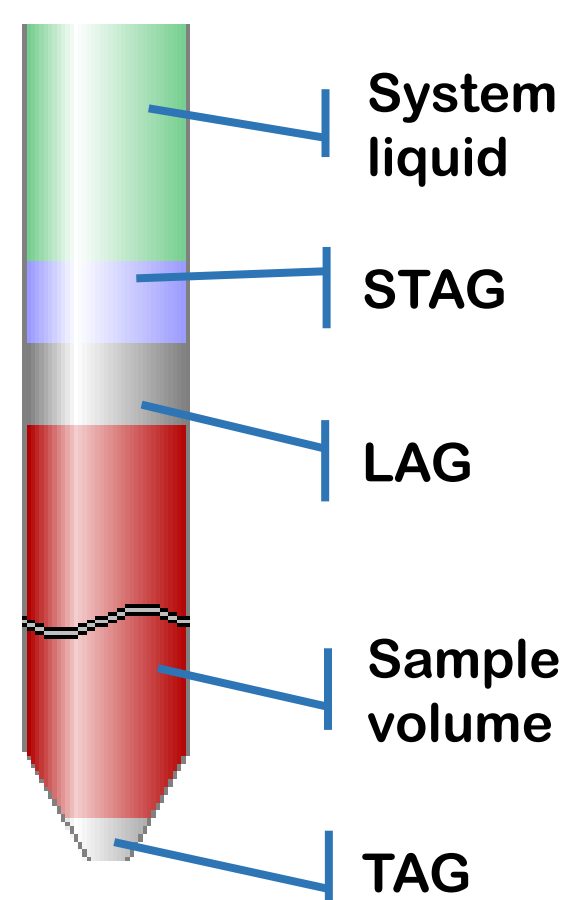
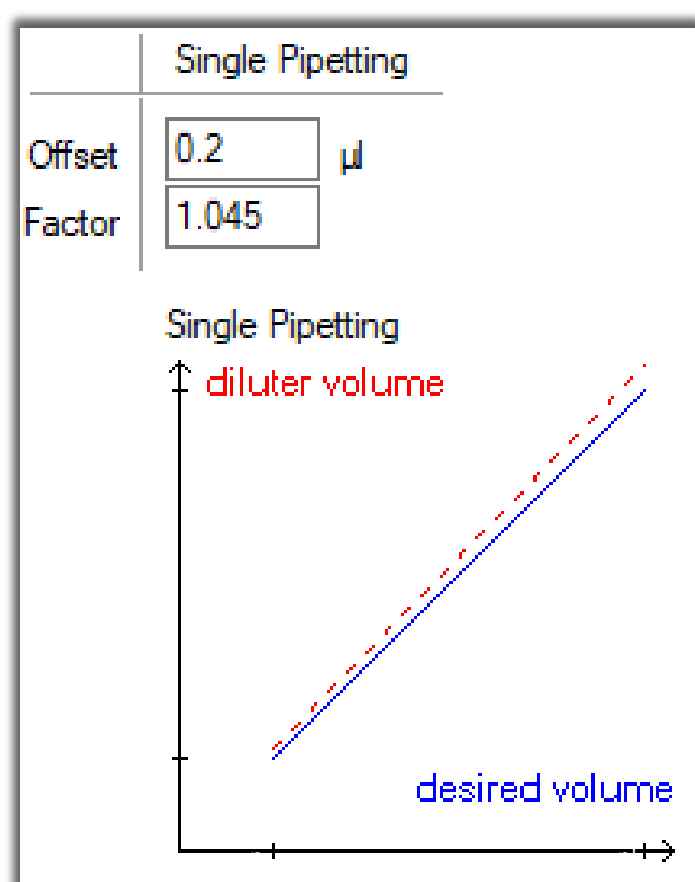
Replace 1000 μ L syringes by 500 μ L syringes and optimization of various parameters:

Calibration parameters :

- The factor
- The offset

$$y = a \cdot x + b$$

Factor: a
 Offset: b



Airgap volume during pipetting :

- STAG : system trailing airgap : to prevent contamination by liquid system
- LAG : Leading Airgap : optimize accurate pipetting
- TAG : Trailing Airgap : to prevent liquid dripping

Pipetting speed :

- The aspiration speed : lower aspiration improve pipetting accuracy
- The distribution speed : high dispense speed is needed to achieve a proper free dispense
- The needle position : in contact or not with the tube

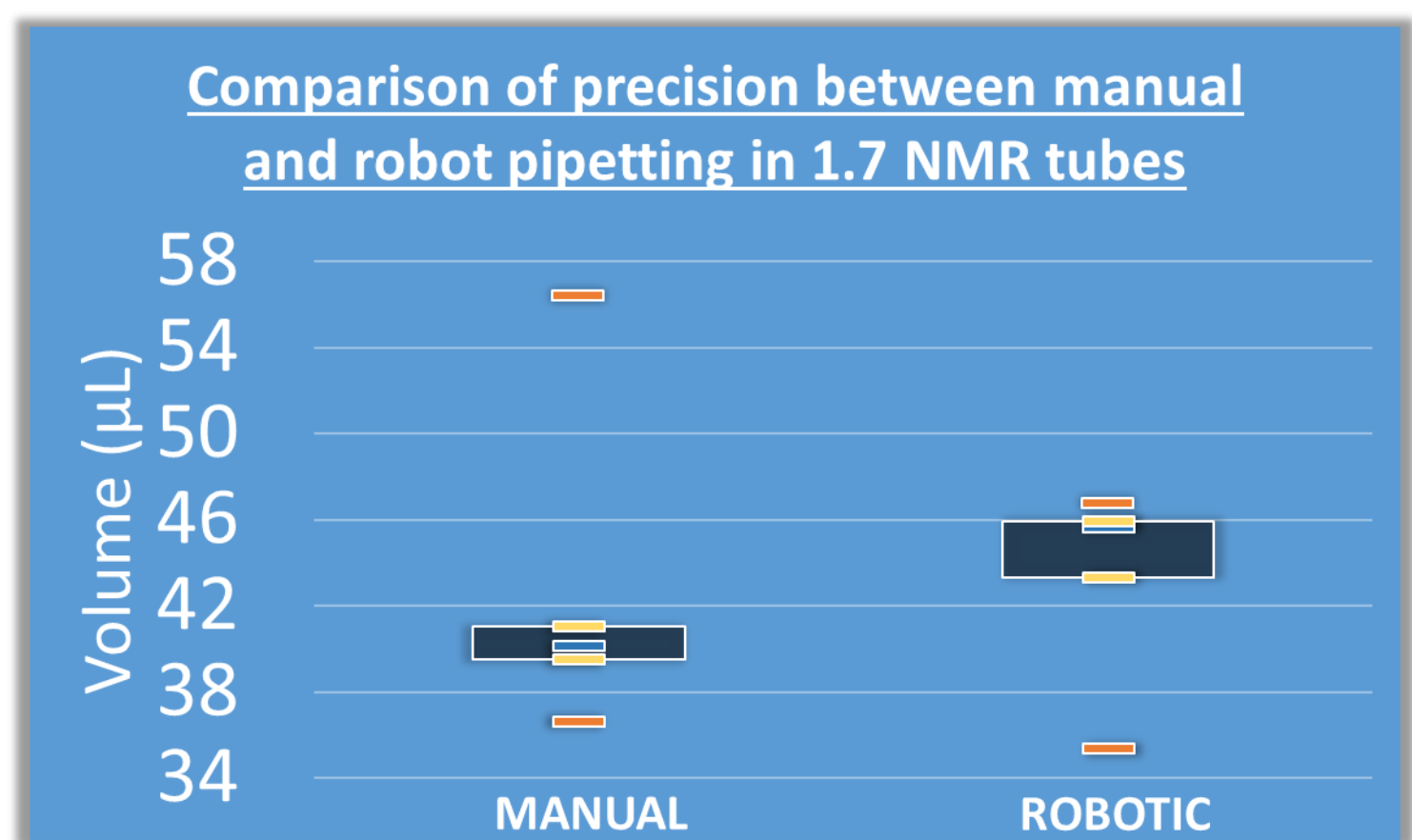
Target volume (μ L)	With 1000 μ L syringes				With 500 μ L syringes			
	100	10	5	1	100	10	3	1
Mean	103.49	10.50	4.78	2.25	100.4	10.27	2.99	1.97
sd	1.04	0.97	0.44	0.6	0.82	0.37	0.08	0.4
Cv (%)	1	9	9	27	0.8	4	3	20

Better precision and accuracy with 500 μ L syringes

2 - Adaptation for new miniaturized devices :

Development of robotic platform protocol to be able to pipette in 1.7 mm and 1 mm NMR tubes

Implementation and validation of a script with use of capillary needles for final dispense of 20 and 45 μ L NMR tubes



NMR tubes filling : measure of final volume in the tube :

	Manual	Robot
MEAN	41 μ L	44 μ L
SD	4.3 μ L	2.6 μ L
MIN	36 μ L	35 μ L
MAX	56 μ L	47 μ L

Better precision and reproducibility with robot
 Faster with robot



NMR Tubes : 5 3 1.7 1 mm

Conclusions

- Pipetting capabilities : range 3 – 480 μ L with a CV max of 4 %.
- Our robotic platform is now capable to fill 5, 3, 1.7 mm and 1 mm NMR tubes

APPLICATIONS : High throughput screening • Provide access to metabolism of cells subpopulation • Replaces humans for repetitive tasks

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