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AUTOMATED PIPETTE CLEANING DRAMATICALLY INCREASES THROUGHPUT IN MULTIPLE PATCH-CLAMP RECORDINGS

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Introduction

- Multiple patch-clamp recordings are the gold standard method to investigate information processing in neural circuits at the sub-cellular resolution.
- Forming a giga seal for the whole-cell recording requires pristine pipette tip: traditionally pipette is changed after each recording and/or its attempt
- In theory, circuit study throughput scales non-linearly according to n×(n−1), where n is number of simultaneously recorded cells (Fig. 1, light grey).
- In practise, yield saturates gradually due to loss of cells from prolonged experiment duration and manual pipette change related movement artifacts (Fig. 1, dark grey).

Impessive increase in multi-patch throughput was presented recently[1] by Dr. Peng and his co-workers from Geiger lab, Charité-Universitätsmedizin, which was achieved by implementing the automated pipette cleaning technique. This application note presents some of the highlights with focus on the practical implementation of the pipette cleaning.

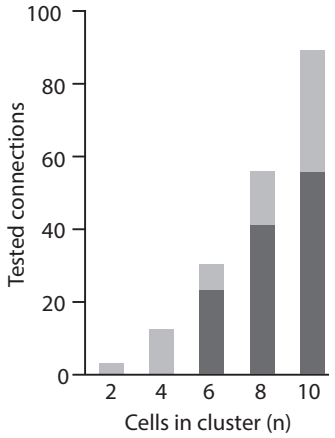


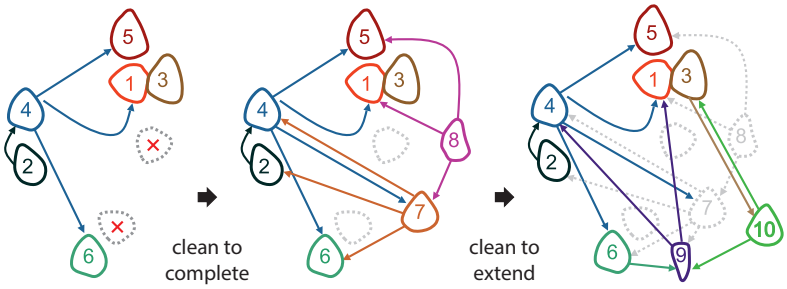
Figure 1. Theoretical and practical yield in traditional multi-patch experiments[1].

Automated pipette cleaning technique

- Invented by Dr. Ilya Kolb and his co-workers from Forest lab, Georgia Tech[2].
- Cleaning enables immediate re-use of the pipette with equal data quality as with pristine tip
- Reduces down-time between the recordings and/or their attempts
- No loss of recordings from manual pipette change and associated movement artifacts
- Proven to be safe to cells: in addition to thorough chemical analysis presented in the original method publication[2], Peng et. al present statisticial analysis showing that normal physiological properties or recording quality are not impaired[1]

74 % increase in throughput!

- Clean-to-complete strategy increased the average cluster size with 8 pipettes from 6.8 to 7.8 cells and success rate increase from 85 % to 97%.
- Clean-to-extend strategy allows highly efficient testing of many further connections
- Combining both strategies increased number of tested connections from 140 ± 24 to 244 ± 52 per animal with 8 pipettes (n = 6 animals).



USEFUL LINKS

Original publication:	https://elifesciences.org/articles/48178
Geiger lab website:	https://neurophysiologie.charite.de/en/research/geiger_group/
Forest lab website:	http://pbl.gatech.edu/

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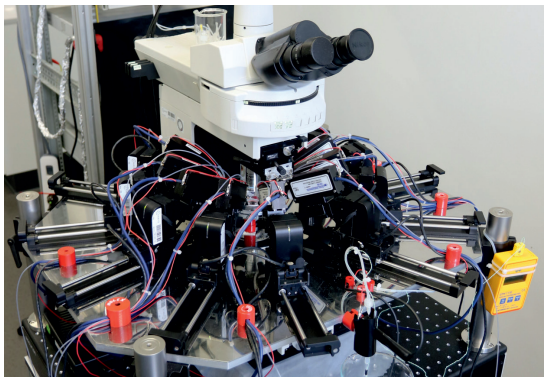
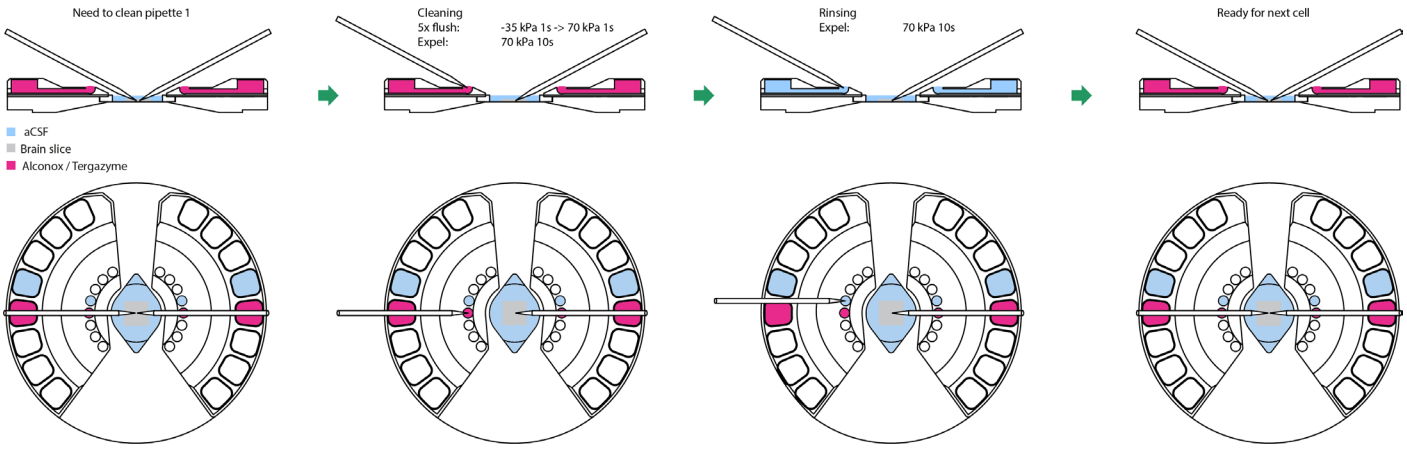


Figure 3. Left, 10 pipette multi-patch setup with automated pipette cleaning[1]. Right, Sensapex uM worksation for automated pipette cleaning and multi-patch.

Practical implementation

- In addition to standard multi-patch setup requirements, implementing the pipette cleaning needs automated pressure controller and sample holder with dedicated compartments for the cleaning and rinsing solutions
- Scaling up and beyond 10 pipettes is possible in well thought setups (Fig 3), but higher overall throughput may follow from using less pipettes but with higher automation level[3,4].
- Cleaning process step-by-step:
  - (1) Used pipette is moved to the dedicated cleaning well filled with Alconox or Tergazyme
  - (2) Vacuum draws cleaning solution to the tip and tip is then flushed by cycling between high pressure and vacuum
  - (3) High pressure pulse is applied to expel all cleaning solution with 10x safety factor.
  - (4) Tip is moved to the rinsing well and some pipette internal solution is expelled through the tip for added safety.
  - (5) Pipette tip is moved accurately back to starting position



Sensapex is the exclusive commercial partner for automated pipette cleaning technology. We provide ready-made products for plug-and-play implementation, incl. 1-click automated cleaning feature.

Learn more at: https://www.sensapex.com/products/umc-automated-pressure-control/

REFERENCES

1. Peng Y et al. High-throughput microcircuit analysis of individual human brains through next-generation multineuron patch-clamp. Elife. 2019 Nov 19;8. pii: e48178.
2. Kolb I et al. Cleaning patch-clamp pipettes for immediate reuse. Sci Rep. 2016 Oct 11;6:35001
3. Kodandaramaiah SB et al. Automated whole-cell patch-clamp electrophysiology of neurons in vivo. Nat Methods. 2012 Jun;9(6):585-7.
4. Kolb I et al. PatcherBot: a single-cell electrophysiology robot for adherent cells and brain slices. J Neural Eng. 2019 Apr 10;16(4):046003.