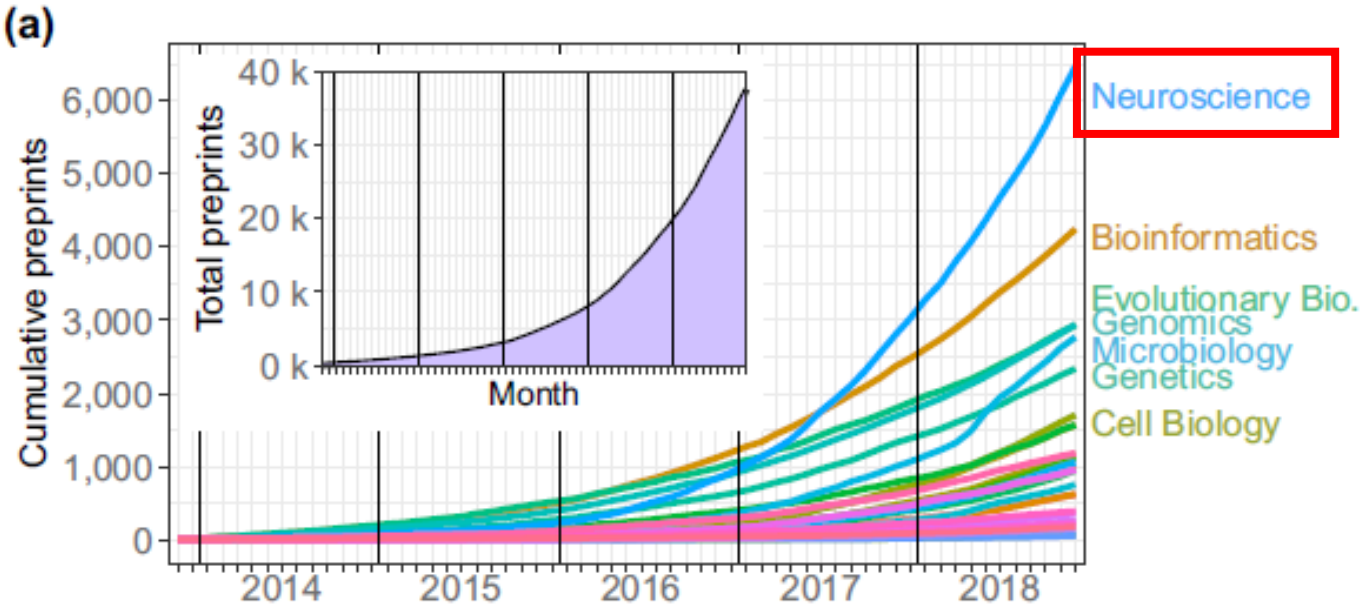
Preprints (*bioRxiv*): Personal experience

SIPBS

Shuzo Sakata

My background/experience

- Neuroscience (systems neuroscience)
- bioRxiv user (9 preprints)



(Abdill and Blenkhman, *eLife* 2019)

NOTE: My experience may NOT be applied in other disciplines

Two viewpoints

- As a reader
- As an author

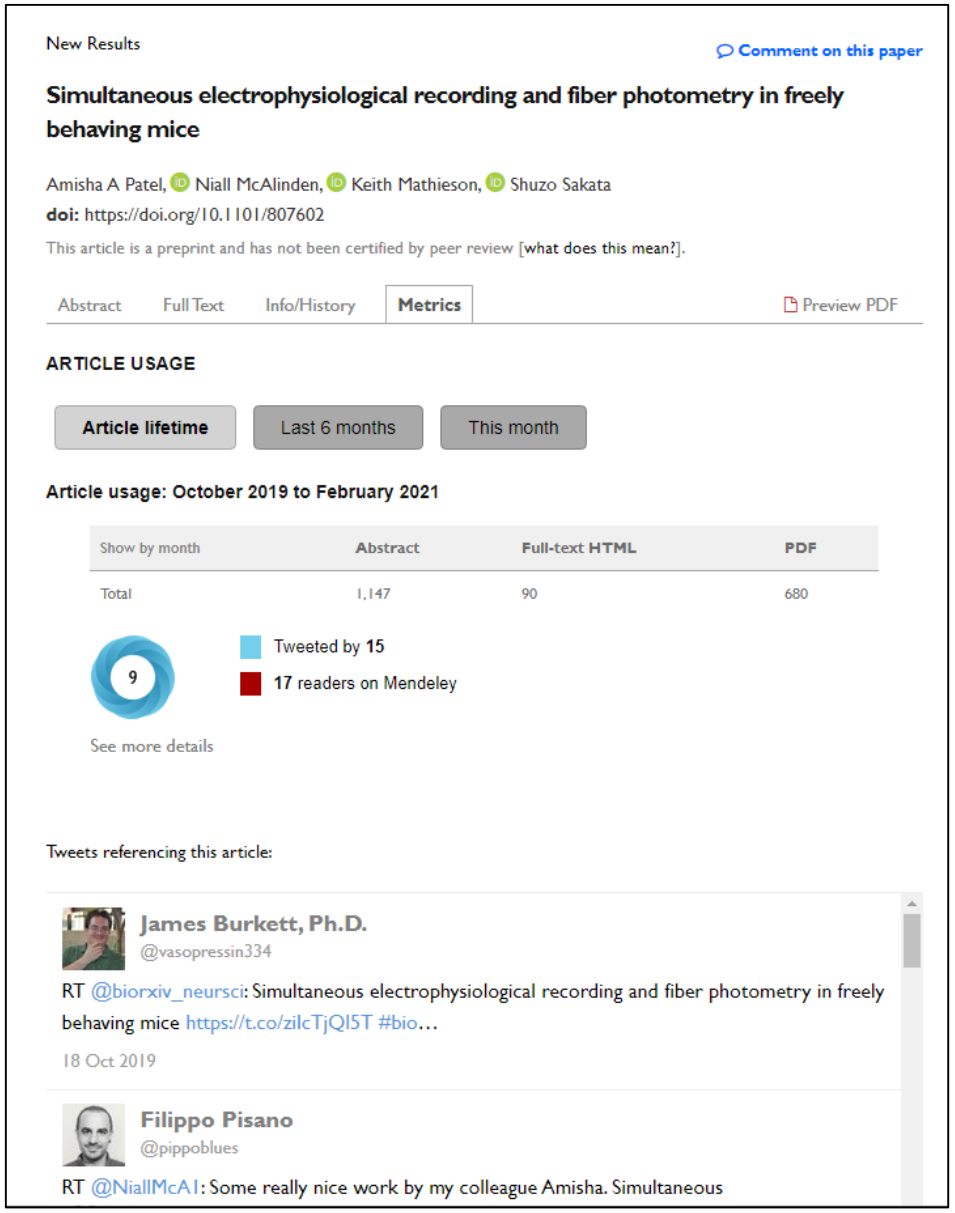
As a reader – treasure hunter

Good platform to train PhD students and Postdocs

- Pros
  - Early access to high-quality manuscripts
  - Good resources for critical analysis
  - Knowing a wide range of styles
- Cons
  - Overwhelming – RSS service can mitigate this to some extent
  - Virtually no quality control - Many low-quality manuscripts

As an author

- Pros
  - **Promoting open science**
  - Easy & Free
  - Quick dissemination – a record
    - Better than “unpublished” or “in prep”
    - Citable
    - Good for ECRs
  - Google Scholar
  - Founders’ recognition (including UKRI)
    - Some referees do check
  - Twitter reactions
- Cons
  - A risk to expose my sloppiness?
  - A risk to end up without a publication?


New Results

Comment on this paper

Simultaneous electrophysiological recording and fiber photometry in freely behaving mice

Amisha A Patel, Niall McAlinden, Keith Mathieson, Shuzo Sakata

doi: https://doi.org/10.1101/807602

This article is a preprint and has not been certified by peer review [what does this mean?].

Abstract | Full Text | Info/History | **Metrics** | Preview PDF

ARTICLE USAGE

Article lifetime | Last 6 months | This month

Article usage: October 2019 to February 2021

Show by month	Abstract	Full-text HTML	PDF
Total	1,147	90	680

9

Tweeted by **15**

17 readers on Mendeley

See more details

Tweets referencing this article:

James Burkett, Ph.D.
@vasopressin334

RT @biorxiv_neursci: Simultaneous electrophysiological recording and fiber photometry in freely behaving mice https://t.co/zilcTjQl5T #bio…

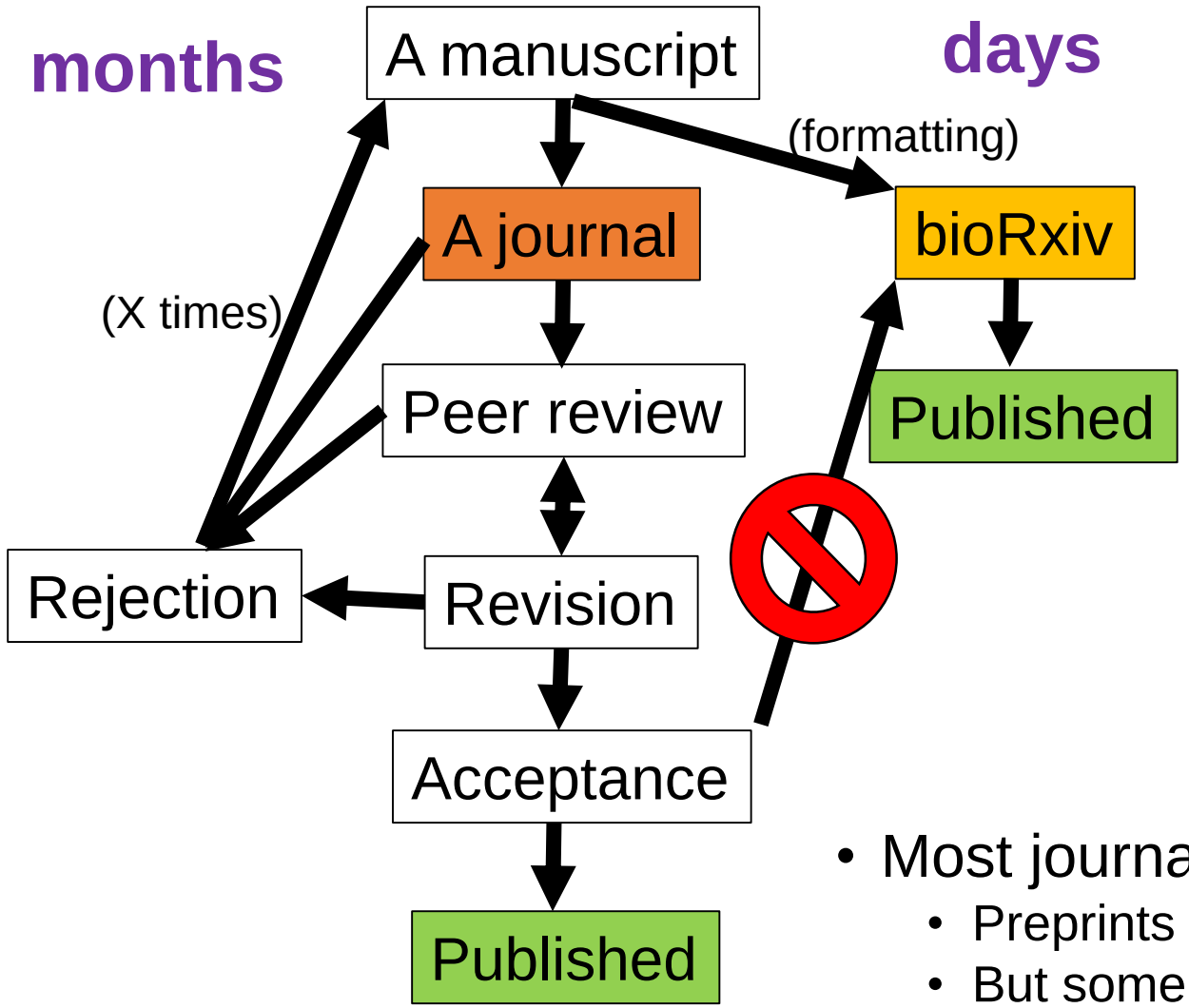
18 Oct 2019

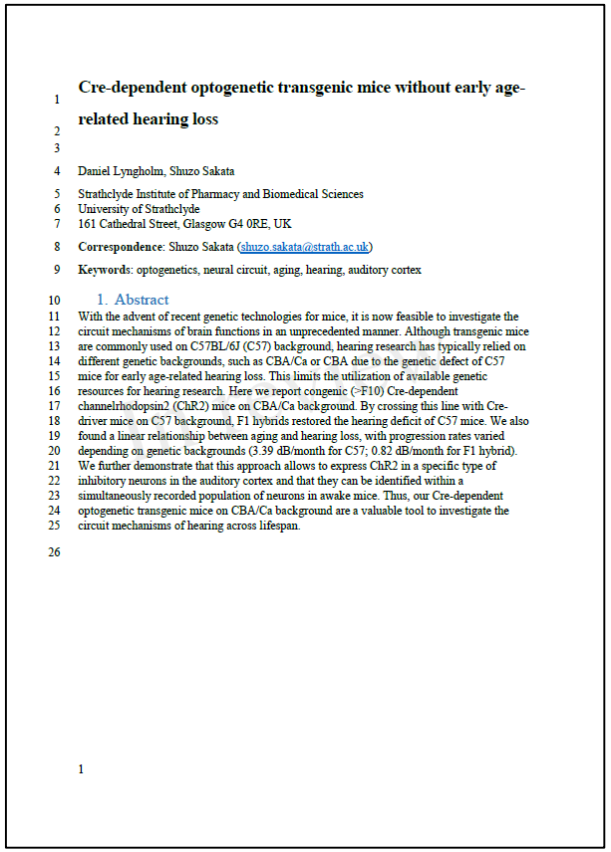
Filippo Pisano
@pippoblues

RT @NiallMcA1: Some really nice work by my colleague Amisha. Simultaneous

Personally I would not support posting an *unpublishable* manuscript.

My current flowchart (Dos & Don’ts)





Cre-dependent optogenetic transgenic mice without early age-related hearing loss

Daniel Lyngholm, Shuzo Sakata

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Keywords: optogenetics, neural circuit, aging, hearing, auditory cortex

1. Abstract

With the advent of recent genetic technologies for mice, it is now feasible to investigate the circuit mechanisms of brain functions in an unprecedented manner. Although transgenic mice are commonly used on C57BL/6J (C57) background, hearing research has typically relied on different genetic backgrounds, such as CBA/Ca or CBA due to the genetic defect of C57 mice for early age-related hearing loss. This limits the utilization of available genetic resources for hearing research. Here we report congenic (>F10) Cre-dependent channelrhodopsin2 (ChR2) mice on CBA/Ca background. By crossing this line with Cre-driver mice on C57 background, F1 hybrids restored the hearing deficit of C57 mice. We also found a linear relationship between aging and hearing loss, with progression rates varied depending on genetic backgrounds (3.39 dB/month for C57; 0.82 dB/month for F1 hybrid). We further demonstrate that this approach allows to express ChR2 in a specific type of inhibitory neurons in the auditory cortex and that they can be identified within a simultaneously recorded population of neurons in awake mice. Thus, our Cre-dependent optogenetic transgenic mice on CBA/Ca background are a valuable tool to investigate the circuit mechanisms of hearing across lifespan.

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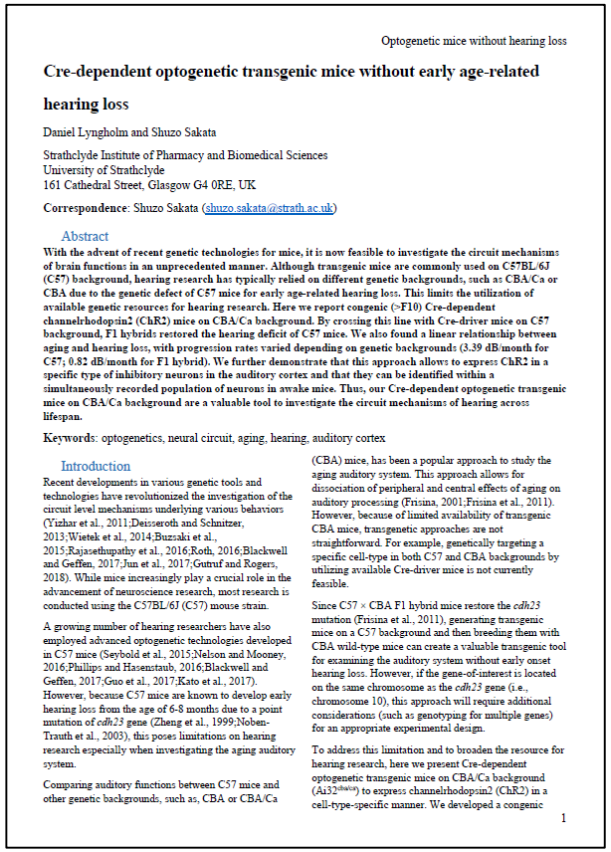

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With the advent of recent genetic technologies for mice, it is now feasible to investigate the circuit mechanisms of brain functions in an unprecedented manner. Although transgenic mice are commonly used on C57BL/6J (C57) background, hearing research has typically relied on different genetic backgrounds, such as CBA/Ca or CBA due to the genetic defect of C57 mice for early age-related hearing loss. This limits the utilization of available genetic resources for hearing research. Here we report congenic (>F10) Cre-dependent channelrhodopsin2 (ChR2) mice on CBA/Ca background. By crossing this line with Cre-driver mice on C57 background, F1 hybrids restored the hearing deficit of C57 mice. We also found a linear relationship between aging and hearing loss, with progression rates varied depending on genetic backgrounds (3.39 dB/month for C57; 0.82 dB/month for F1 hybrid). We further demonstrate that this approach allows to express ChR2 in a specific type of inhibitory neurons in the auditory cortex and that they can be identified within a simultaneously recorded population of neurons in awake mice. Thus, our Cre-dependent optogenetic transgenic mice on CBA/Ca background are a valuable tool to investigate the circuit mechanisms of hearing across lifespan.

Keywords: optogenetics, neural circuit, aging, hearing, auditory cortex

Introduction

Recent developments in various genetic tools and technologies have revolutionized the investigation of the circuit level mechanisms underlying various behaviors (Yizhar et al., 2011;Deisseroth and Schnitzer, 2013;Wietek et al., 2014;Buzsaki et al., 2015;Rajasethupathy et al., 2016;Roth, 2016;Blackwell and Geffen, 2017;Jun et al., 2017;Gutruf and Rogers, 2018). While mice increasingly play a crucial role in the advancement of neuroscience research, most research is conducted using the C57BL/6J (C57) mouse strain.

A growing number of hearing researchers have also employed advanced optogenetic technologies developed in C57 mice (Seybold et al., 2015;Nelson and Mooney, 2016;Phillips and Hasenstaub, 2016;Blackwell and Geffen, 2017;Guo et al., 2017;Kato et al., 2017). However, because C57 mice are known to develop early hearing loss from the age of 6-8 months due to a point mutation of *cdh23* gene (Zheng et al., 1999;Noben-Trauth et al., 2003), this poses limitations on hearing research especially when investigating the aging auditory system.

Comparing auditory functions between C57 mice and other genetic backgrounds, such as, CBA or CBA/Ca (CBA) mice, has been a popular approach to study the aging auditory system. This approach allows for dissociation of peripheral and central effects of aging on auditory processing (Frisina, 2001;Frisina et al., 2011). However, because of limited availability of transgenic CBA mice, transgenetic approaches are not straightforward. For example, genetically targeting a specific cell-type in both C57 and CBA backgrounds by utilizing available Cre-driver mice is not currently feasible.

Since C57 × CBA F1 hybrid mice restore the *cdh23* mutation (Frisina et al., 2011), generating transgenic mice on a C57 background and then breeding them with CBA wild-type mice can create a valuable transgenic tool for examining the auditory system without early onset hearing loss. However, if the gene-of-interest is located on the same chromosome as the *cdh23* gene (i.e., chromosome 10), this approach will require additional considerations (such as genotyping for multiple genes) for an appropriate experimental design.

To address this limitation and to broaden the resource for hearing research, here we present Cre-dependent optogenetic transgenic mice on CBA/Ca background (Ai32$^{flx/wt}$) to express channelrhodopsin2 (ChR2) in a cell-type-specific manner. We developed a congenic

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- Most journals in my field allow posting preprints
  - Preprints = *not-yet-accepted* manuscripts
  - But some explicitly prohibit posting a **revised** manuscript
- Accepted manuscript → Pure

Conclusion as an author

- Support Open Science? Suitable for Open Science?
  - Yes → bioRxiv or other preprint servers
  - No → a conventional path
- Better for a publishable, but *not-yet-accepted* manuscript