CeAid: A smartphone application for logging and plotting C. elegans assays

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Abstract

C. elegans is used as a model organism to study a wide range of topics in molecular and cellular biology. Conventional C. elegans assays often require a large sample size with frequent manipulations, rendering them labor-intensive. Automated high-throughput workflows may not be always the best solution to reduce benchwork labor, as they may introduce more complexity. Thus, most assays are carried out manually, where logging and digitizing experimental data can be as time-consuming as picking and scoring worms. Here we report the development of CeAid, C. elegans Application for inputting data, which significantly expedites the data entry process, utilizing swiping gestures and a voice recognition algorithm for logging data using a standard smartphone or Android device. This modular platform can also be adapted for a wide range of assays where recording data is laborious, even beyond worm research.

Introduction

The nematode C. elegans is a powerful multicellular model organism that is used to study genetic pathways controlling cellular processes such as development, reproduction, and age-related decline. This is due to its small size, short generation time, genetic amenability, and conservation of cellular and molecular processes across species. Many C. elegans protocols require a large sample size. Much progress has been made in assay automation utilizing liquid workflows, robotic imaging platforms, and data analysis software. These tools enable users to carry out high-throughput genetic and chemical screens. For instance, advanced tracking algorithms coupled with imaging platforms were developed to automate data acquisition and analysis of C. elegans body shape and locomotion. WormFarm and WorMotel are also examples of microfluidic platforms that use automated algorithms for device operation, image processing, and data analysis focusing on expediting life span assays. These tools are generally assay-specific, and the development of novel high-throughput techniques is frequently needed for new assays or protocols. Additionally, complete automation of some assays, such as fluorescence imaging and complex behavior tracking, may be much harder to achieve. In some cases, automation of experiments with recurring operational steps, such as assays of brood size and reproductive span, require daily data collection and cannot be easily scaled. Microfluidics technologies have proven to be a powerful tool for handling complicated protocols. However, fabrication and operation of chips may require an engineering background and can be time-consuming, often halting the further use of these tools at the proof-of-concept technological validation step. Overall, traditional methods for the culture of C. elegans on solid agar plates, picking worms using a platinum wire, and scoring them manually is an invaluable part of worm research. Thus, aiding researchers to expedite these manual tasks would be worthwhile.

In many standard manual assays with a large sample size, the researcher has to frequently switch between pick and pen to record data, searching for the proper location on the datasheet. The final step of digitizing a massive data log can often be as labor-intensive as performing the assay itself. To minimize the amount of time that the experimenter spends recording data, we have developed CeAid (C. elegans Application for inputting data) to automate the data entry process, which can be used for most manual assays in worms. Using features such as voice command, swiping, and tap gestures, CeAid does not require the user to shift focus to the pen and paper throughout the assay; all that is needed is a standard smart phone. We have utilized CeAid to log conventional C. elegans assays such as life span (LS), reproductive span (RS), brood size, and choice assays. The source code along with the APK file for CeAid are available at https://github.com/murphylab-Princeton/CeAid and https://murphylab.princeton.edu/CeAid.

Results

Users can interact with CeAid through voice command, swiping, and tap gestures while the talk-back feature reconfirms the user’s input and declare the state of the app for receiving new data. Slider bars and embedded Numpad are also integrated into CeAid platform, allowing users to input data manually. New experiments can be set up by adding relevant information (Figure 1a-b). Scrolling through the expandable list of created experiments (Figure 1c) and tapping on any assay image, users are presented with a gallery view of color-coded icons showing the stored data or vacant slots (Figure 1d-e).
Reproductive span assay. Female reproductive cessation is one of the earliest hallmarks of age-related decline. C. elegans has proven to be a useful model organism to better understand conserved mechanisms that regulate reproductive aging. The duration of the progeny production period can be measured by checking whether hatched progeny exists on plates each day during the reproductive period. Swiping up or down on CeAid, the user can record if an individual worm is reproductive on a specific day, while a single tap can be used to censor the worm from the experiment, if needed (Figure 2c). More censoring options/notes are also provided at the bottom of the screen. After initiating these commands, the talk-back algorithm confirms input data and automatically prompts the user to the next sample. Swiping left and right enables navigation through samples and double-tap and long-press switch the day of the experiment. In LS assays where data are needed for individual worms, the app provides a similar platform as RS assay to instead log dead or alive states (Figure 2d).

Brood size assay. The number of live progeny produced daily can also be used to study reproduction. Wild-type hermaphrodites use their limited number of self-sperm and can produce about 250 self-fertilized progeny, while mated animals can produce a substantially larger number. Brood size assays within CeAid incorporate both voice recognition machine and Numpad to record the number of progeny produced (Figure 2e). Double-tap initiates listening algorithm while long-press censor the sample on a specific day. The number of unhatched eggs and unfertilized oocytes can also be recorded when slider bars appear on the sides of the screen. Similar to the LS assay, vertical and horizontal swiping provide navigation through samples and days of the experiment, respectively.

Choice assay. In choice assays, animals choose between two spots on agar plates, which can be used to measure behavioral phenotypes such as dietary preference, chemotaxis, olfactory learning behavior, and avoidance of pathogenic bacteria. To record choice assay data, the user can activate the voice recognition algorithm by double-tapping on screen or, alternatively, use an embedded Numpad at the bottom of the screen (Figure 2f). Furthermore, swiping gestures enable navigation through recorded samples.
Visualization. Recorded data can be plotted within CeAid or exported to an Excel file for further statistical analysis (Figure 3). Using on-demand plotting, the trajectory of the experiment can be visualized while it is happening prior to analysis using statistics programs (Figure 3a). The demo examples are also integrated into the app and can be produced on the main activity page.

Conclusion

CeAid is developed to automate manual data entry procedures for *C. elegans* assays through a series of highly simplified steps. This open-source android application is modular and functions for tap and swipe gestures along with voice recognition algorithm, slider bars, and embedded Numpad can be adapted for newer scoring assays. Overall, eliminating the need to shift the user’s focus to pen and paper throughout the experiment can significantly expedite worm research.
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Figure 3. On-demand plotting. (a) Survival curve of an undergoing experiment for sample populations of mated and unmated animals. (b) The reproductive span of self-fertilized N2 and eat-2 worm strains. (c) Wild-type worms exposed to P. aeruginosa (PA14) beginning on Day 1 of adulthood produce less progeny compared to whole-life OP50 fed worms. Swiping left/right navigates to plots for daily number of unhatched eggs and unfertilized oocytes. (d) Wild-type worms were trained on different pathogenic bacteria. Following training, an aversive learning assay was conducted to determine worms’ food preference compared to control food. Choice index = (number of worms on OP50 – number of worms on bacteria)/(total number of worms). The box plot shows minimum, 25th percentile, median, 75th percentile, maximum. The number of conditions to be plotted can be set and swiping left/right provides the capability to navigate through them.

Acknowledgments
S. S. and C.T.M. designed the layout for the app. S. S. developed the code. R.S.M. provided demo data. S. S. and C.T.M. wrote the manuscript. C.T.M. supervised the project and acquired funding. We thank Murphy lab for discussion, particularly Rachel Kaletsky, Cheng Shi, Vanessa Cota, Will Keyes for great suggestions and sharing data. This work was supported by the Glenn Foundation for Medical Research award to C.T.M. (GMFR CNV1001899) and NIH award RF1AG057341 (NIA).

Declaration of Interests
The authors declare no competing interests.

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