

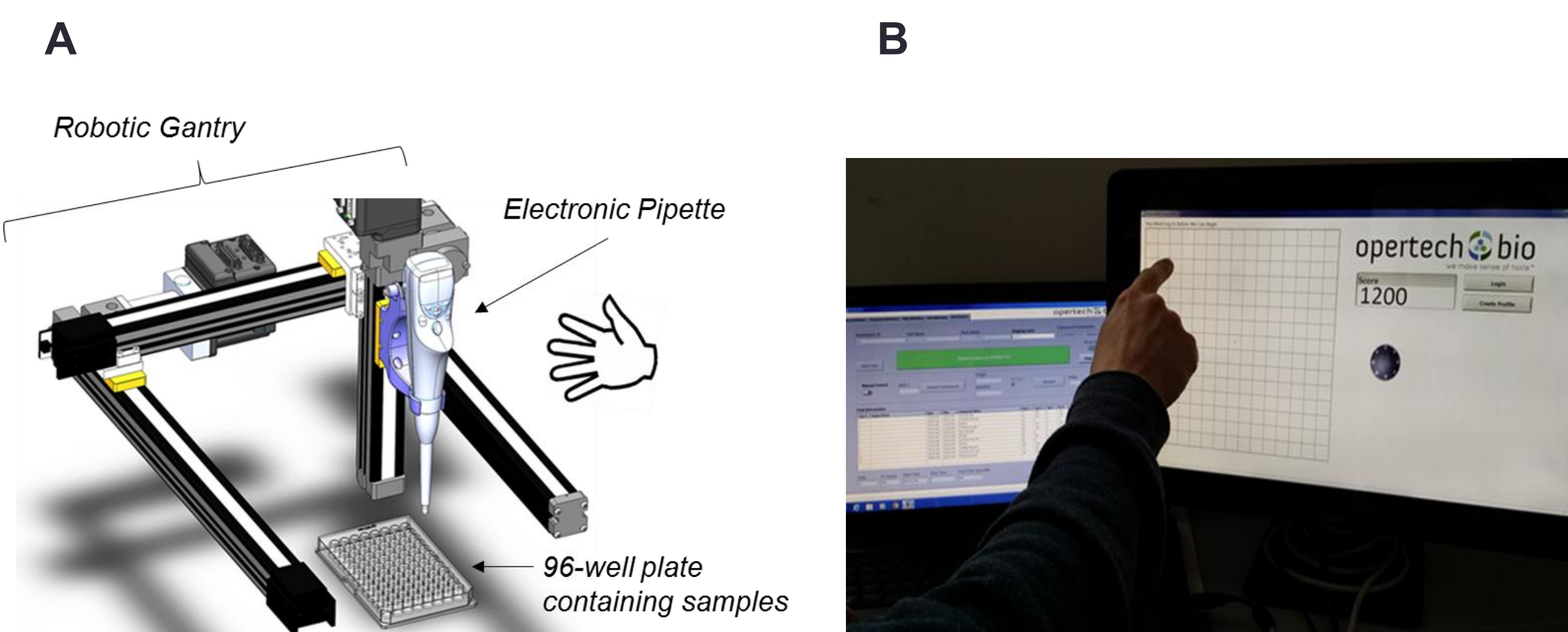
A New Paradigm for Human Taste Measurement

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ABSTRACT

We previously developed a high throughput system for in vivo measurement of taste quality and palatability using rats as subjects (Palmer et al, 2013, PLoS ONE). We now have extended this technology to creation of a new paradigm for taste measurement in humans. The system is fully automated and is comprised of a robotic sample delivery system, a touch-sensitive display (TSD) that records the subjects' responses, and a command computer that runs subject-interactive algorithms and communicates with a database. The algorithms that operate the taste testing method are "gamified" - structured according to game play and game mechanics. Subjects are trained how to use the system through the interactive algorithms and are given minimal instruction. The samples (200-500 ul each) are drawn from a single randomly-selected well of a 96-well plate by an automated pipette clipped to a robotic gantry. The gantry moves the pipette to the subject who then removes the pipette and self-administers the solution. A set of taste-stimulus standards are mapped to specific locations in the visual field of the TSD, and subjects are trained by the algorithms to touch a location on the TSD for a reward after tasting the sample. The rewards are virtual poker chips with point values that are directly remunerated for actual currency at the end of a session. The algorithms are designed to incorporate principles of operant conditioning and signal detection theory and are structured to provide consequences to the subject's response on each trial. Thus taste-testing performance and rate of testing are incentivized. Subjects typically complete a 96-trial session in 45-60 minutes with high performance accuracy and test-to-test reproducibility. The software is designed to accommodate flexibility in experimental design so that a large array of test protocols can be operated under the interactive algorithms.

AUTOMATED SYSTEM FOR HIGH THROUGHPUT MEASUREMENT OF HUMAN TASTE

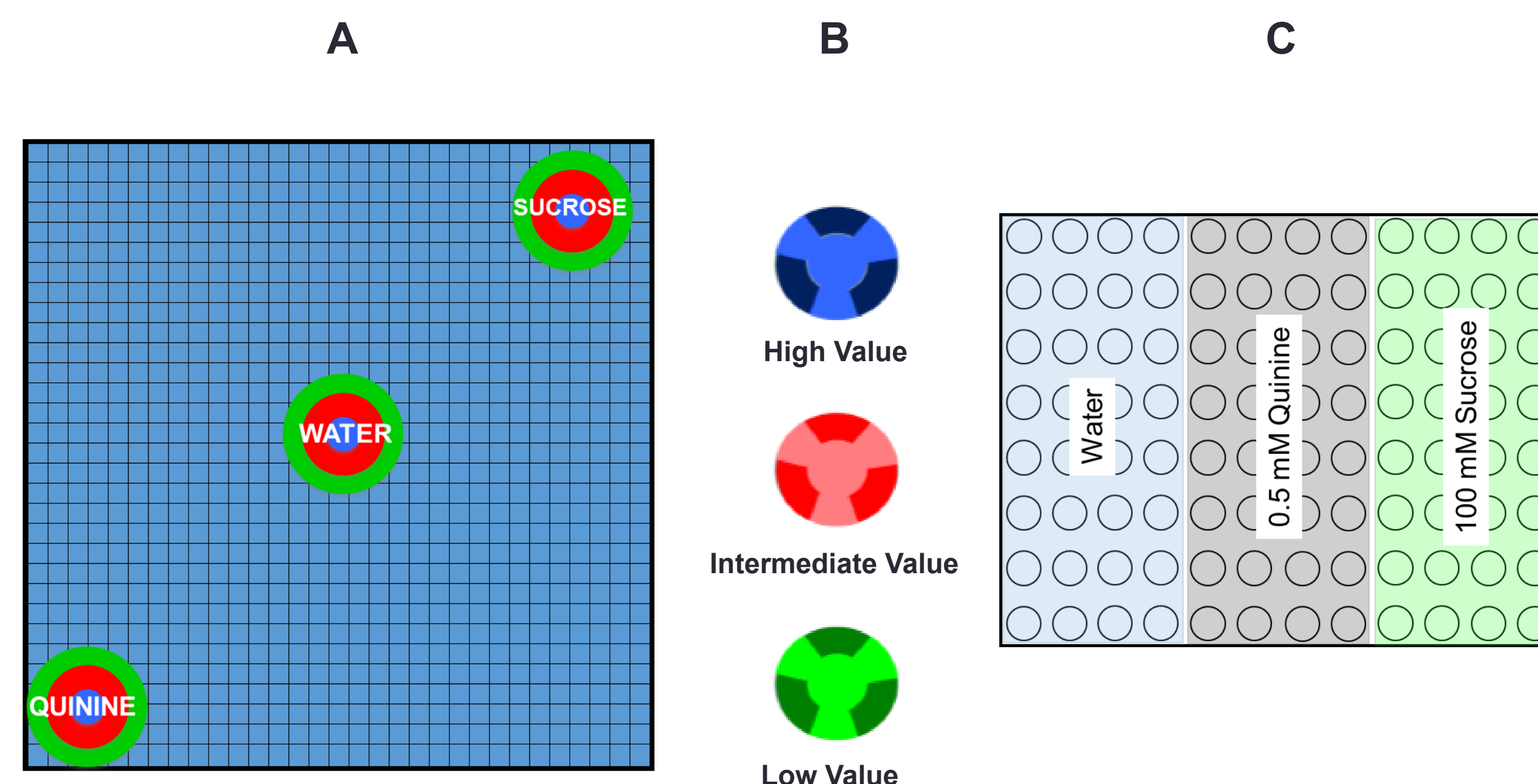


The TāStation® is a portable work station with an automated system for delivering small samples (usually between 200 and 500 ul) in rapid succession to a seated subject. The subject is not given explicit instruction on how to respond, but is trained through an interactive algorithm to make responses that are dependent on his or her ability to detect and distinguish taste stimuli. The response device is a touch-sensitive monitor. Through the algorithm, which operates like a game, subjects learn to associate specific locations on the monitor with a taste stimulus. Touch responses on the screen are rewarded with an incremental point system that incentivizes both sensory acuity and rate of responding.

A) Robotic gantry moves an automated pipette over a 96-well plate. The pipette is lowered into a randomly selected well and withdraws a fixed volume of 200 - 500 ul. The gantry then presents the pipette to subject. The subject is instructed by the algorithm to remove the pipette and self-administer the content of the pipette to the tongue. The gantry is housed within a cabinet (not shown) with a portal through which the pipette is presented.

B) Subjects are prompted by the algorithm to search for poker chips buried in a visual field; the taste stimulus is a clue to their location. The subject touches the screen at a location guided by the taste of the antecedent stimulus. Response-reinforcement contingency is absolute on control trials (taste standards). On test article trials—those for novel stimuli—responses are reinforced.

ENTRY LEVEL TRAINING MODULE: CALIBRATION, GRADED REWARD VALUE



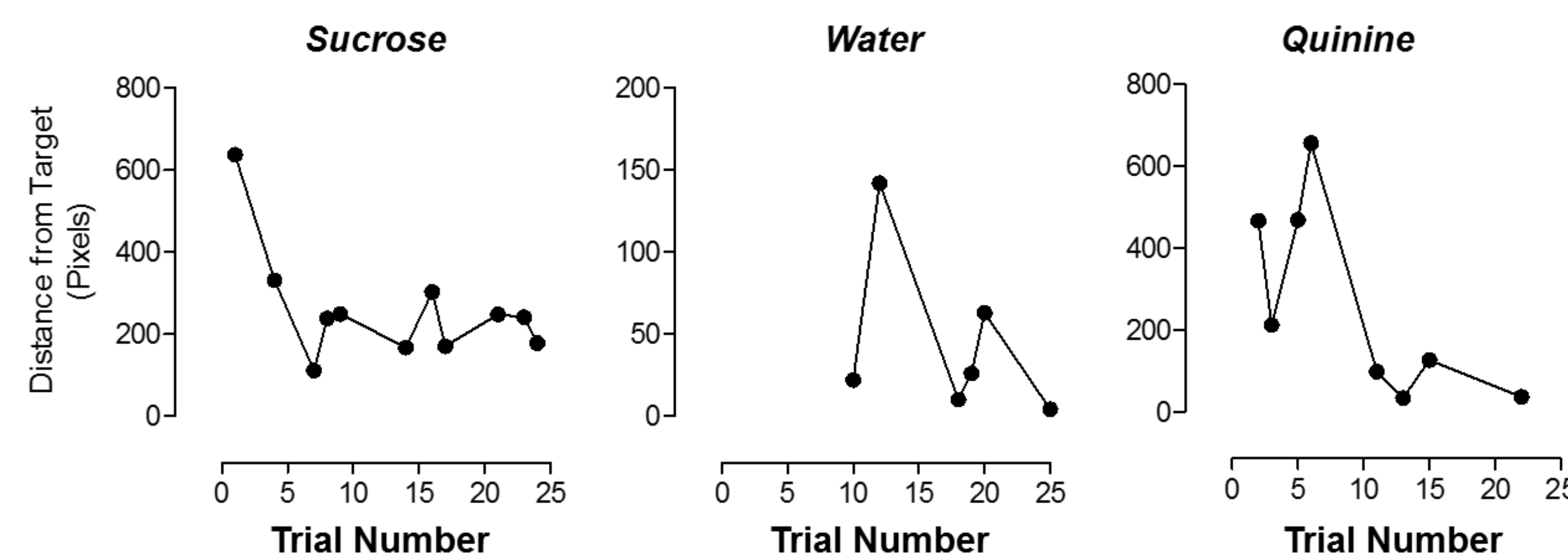
Subjects are introduced to the TāStation® algorithm by an entry level training program that is calibrated by a few taste stimuli. Number of different stimuli, configuration of their locations, and area of each target are input variables under the control of the test administrator.

A) In this example, the tastes of sucrose (sweet and palatable), quinine (bitter and unpalatable), and water (neutral) are mapped to specific coordinates on a Cartesian grid appearing on the display. Targets are invisible to the subject, who must discover their locations through trial-and-error.

B) Touch responses made within the target areas on control (standard taste) trials are reinforced by the appearance of a poker chip on the display. There are three poker chip values (high, intermediate, and low)—magnitude of point value is an input variable set by the test administrator prior to the start of a session. Points accumulate across trials. Consequences of errors (responses made outside of the target areas) can be either neutral or negative. Negative consequences include a time-out, in which the display dims and a delay before the next trial, is imposed, and/or subtraction of points earned.

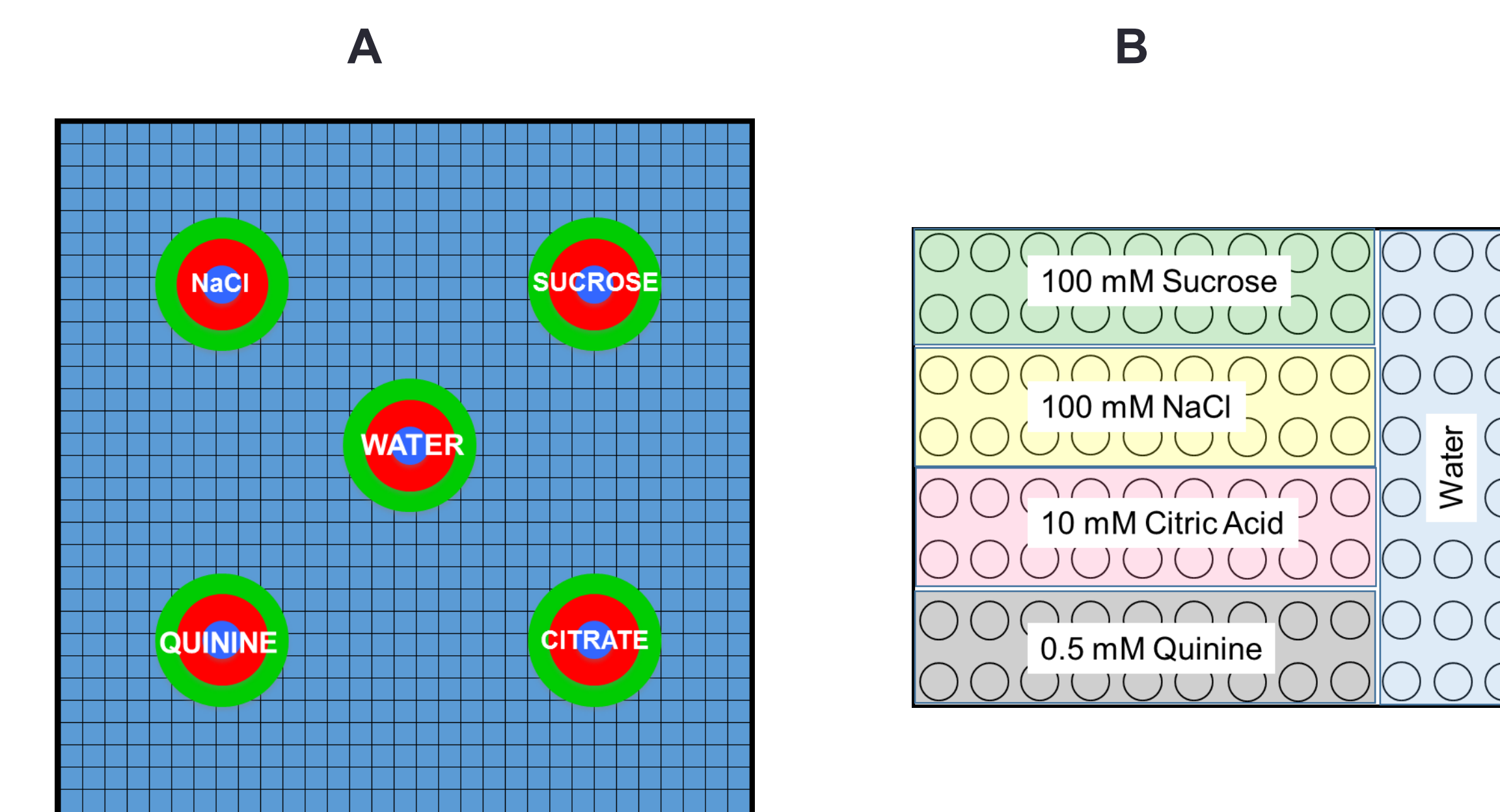
C) Configuration of the 96-well plate used for the training module

TYPICAL TRAINING RESULTS FROM SINGLE SUBJECT



Subjects quickly learn the concept and fundamental rules of the game. In this example, the graph shows the results of a subject that exceeded a criterion of 700 points within 25 trials. Surpassing the criterion qualified the subject for advancement to a higher challenge level in which additional taste stimuli were included in the algorithm.

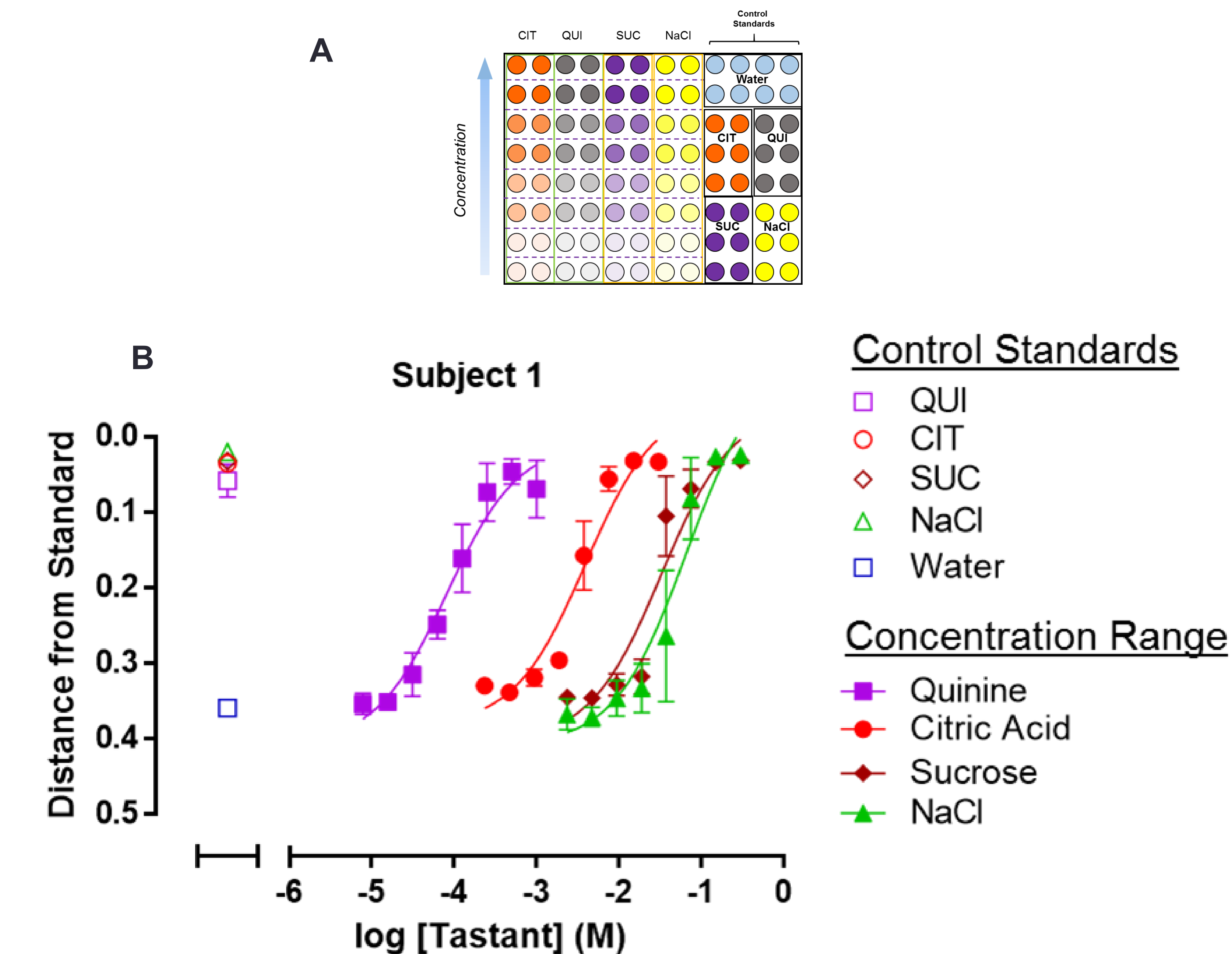
CALIBRATION FOR LEVEL 2 TRAINING MODULE



A) After proficiency in performance is achieved in the entry level training mode, subjects are advanced to a higher level. In this Level 2 Training Module the touchscreen is calibrated with the addition of salty and sour taste standards.

B) Configuration of the 96-well plate used for the training module.

SINGLE SUBJECT, SINGLE TEST SESSION, 4 CONCENTRATION-RESPONSE FUNCTIONS FOR TASTE



A) Configuration of the 96-well plate used to generate concentration-response functions for basic tastes.

B) Concentration response functions were generated in single test sessions using the plate shown in (A). Data are plotted as the average for each point across two consecutive test sessions, error bars = SEM. Curves were fit by non-linear regression (GraphPad Prism). Control standards: QUI=0.5 mM quinine, CIT=10 mM citric acid, SUC=100 mM sucrose, NaCl=100 mM NaCl, and water.