

# Automated High Throughput Objective Assessment of Human Taste Palatability Predictive of Consumption

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## ABSTRACT

Psychoactive drugs are characterized by stimulus properties that generate qualitative interoceptive stimuli, and by reinforcing properties that promote or suppress drug consumption. Similarly, tastant agonists, chemicals that stimulate T1R and T2R receptors expressed in taste buds, also can be thought of as carrying stimulus properties which generate taste qualities, and reinforcing properties that impact tastant consumption. Objective measure of taste quality in both humans and animals is obtained from taste discrimination assays, but objective quantification of “palatability”—the property that determines tastant consumption—only is evident in animal models. We previously reported a high throughput automated system for human taste discrimination, the TaStation™. We have further developed the TaStation™ for objective measurements of palatability that predict tastant consumption. The basis of the method is a game in which subjects spend money from a limited virtual “bank account” to create an “ideal plate”—a 96-well plate that, from the subject’s perspective, contains the best-tasting set of samples. The samples (200 µl each) to be evaluated are randomly presented to subjects in replicates, drawn by an electronic pipette from another 96-well plate, the “source plate.” Subjects self-administer each sample from the pipette to the tongue, then select one of two buttons, labelled “Include” or “Exclude,” appearing on a touch-sensitive display. A button-touch indicates a subject’s intention to include the sample in, or exclude it from, their ideal plate. A subsequent touch on a monetary scale (range = \$0.00 to a pre-set maximum) also appearing on the display indicates the price the subject will pay (withdrawn from their bank account) to actuate the inclusion-exclusion operation. The amount spent is equated with a probability that the inclusion-exclusion choice will be carried forward—maximum allowed expenditure buys a probability of 1.0 guaranteeing execution of the subject’s choice, whereas a zero expenditure results in a probability of 0.5 that the sample will be either included or excluded. Samples for which a subject spends the highest amounts either predominate (“Include”) or are absent (“Exclude”) in the final ideal plate. Approximately half of the samples for which a subject spends nothing appear in the final ideal plate. After 96 such trials, the completed ideal plate is submitted to a computer-generated virtual market that rewards the subject for their ideal plate creation efforts by returning a monetary value on the plate content. At the game’s conclusion, the subject is remunerated in actual money for the amount remaining in their bank account and for the amount returned by the virtual market. The rewards are balanced to ensure incentive for spending the limited bank account resources toward ideal plate design. A subject’s taste “preferences” can readily be discerned from the final ideal plate configuration, and the amounts spent for each tastant operationally quantifies palatability. In a series of tests, the amounts spent per sample closely mirrored actual volumes consumed by each subject measured from 30 ml samples of the same tastant solutions, thereby providing a validation of the TaStation™ method for objective quantification of palatability.

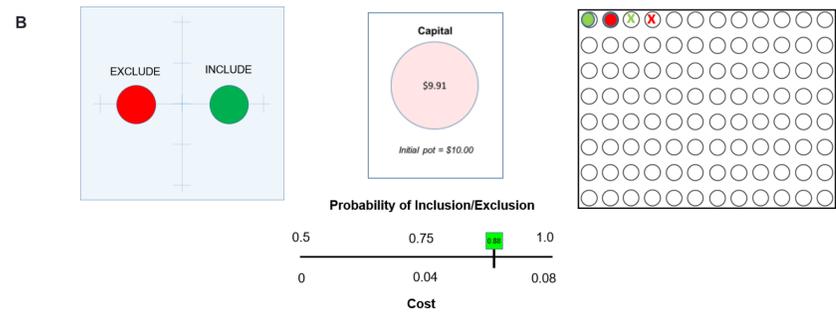
## AUTOMATED SYSTEM FOR HIGH THROUGHPUT ASSESSMENT OF HUMAN TASTE PALATABILITY

The TaStation™ is a portable work station with an automated system for delivering small samples (usually 200 µl) in rapid succession to a seated subject.



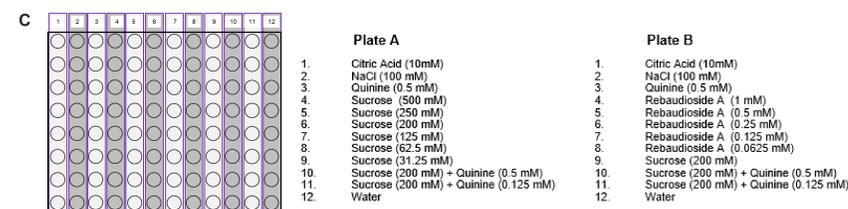
(A) A robotic gantry lowers an automated pipette into a 96-well plate situated on an x-y motion table. The pipette is lowered into a randomly selected well and withdraws a fixed volume of 200 µl. The subject is instructed by the algorithm to remove the pipette and self-administer the content of the pipette to the tongue. In this method, subjects are instructed to spend money from a limited virtual “bank account” to create an “ideal plate”—a 96-well plate that, from the subject’s perspective, contains the best-tasting set of samples from the “source plate.” At the end of the session, a “virtual market” values the subject’s “ideal plate” design.

## INTERACTIVE ALGORITHM



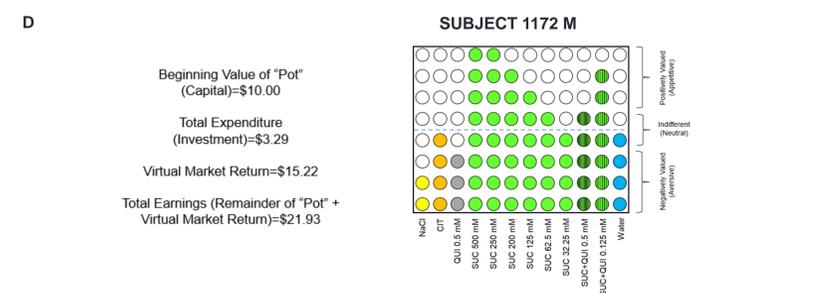
(B) A visual display appears on the touch-sensitive monitor presenting a choice of action between “include” or “exclude.” Upon selecting the choice of action, an image depicting the “pot” or capital amount given to the subject at the start of the game is displayed. The “pot” is an account provided to the subject from which to spend on each action of inclusion or exclusion. Also appearing on the screen is a sliding bar on a scale that depicts a monetary value (ranging from \$0.00 to \$0.08) and a probability (ranging from 0.5 to 1.0). The subject moves the bar to a monetary value (and corresponding probability) that is dependent on the degree to which the subject desires a particular outcome. Expenditures ranging in between the extremes correspond to increasing probabilities that the choice of action would be carried out as desired. The subject could pay the maximum allowed for a trial (in this case, \$0.08) to guarantee (i.e., probability = 1.0) that the sample would be included in (if highly appetitive) or excluded from (highly aversive) the plate he or she is creating. An expenditure of \$0.00 results in execution of a choice of action with a probability of 0.5 (random) and thus is an indication of indifference toward the sample. Capital available to the subject is adjusted as the bar moves. An 8x12 grid is continuously displayed on the computer monitor to keep track of actions and outcomes as the subject progresses through each trial. A colored chip or “X” appeared in the wells; a chip indicates inclusion, an x indicates exclusion from the plate; green color indicates the desired outcome, whereas red color indicates the undesired outcome. Upon completion of the test session, the subject’s created plate is automatically entered into a virtual (computer-generated) market that judges and consequently places a monetary value on the quality of the plate and returns a monetary reward to the subject for the plate’s design. This step was necessary to incentivize the investment of capital by the subject (withdrawn from the subject’s “pot”) in the creation of the plate. Immediately after the display of the market value, the subject was compensated with actual money equal to the remaining sum in the subject’s “pot” plus the market value.

## CONFIGURATION OF 96-WELL “SOURCE PLATE”



(C) Two sets of 11 taste stimulus solutions were created from various concentrations of citric acid, quinine, NaCl, sucrose, Rebaudioside A, or mixtures of these. Each solution of a set was dispensed in 8 wells of a 96-well plate according to the general configuration shown in the figure. In each plate, 8 wells also were designated for water.

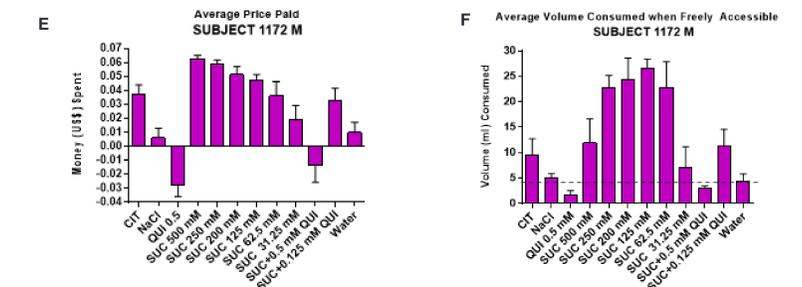
## FINAL “IDEAL PLATE” CREATED BY SUBJECT



(D) Example of a final plate created by subject 1172M from source “Plate A” in the TaStation consumption model game. Colored wells indicate the presence of a taste stimulus solution; wells with no color indicate empty wells. The occupancy of a well was determined probabilistically by the computer algorithm using the monetary value and corresponding probability of choice-execution set by the subject on each trial. Starting value of the subject’s pot was \$10.00, and the cumulative amount spent by the subject in the plate’s creation was \$3.29. The Virtual Market returned a value of \$15.22, and that value was added to the remaining sum in the subject’s “pot” for total earnings of \$21.93 (paid to the subject in actual currency at the completion of the sessions).

## PREDICTIVE OF CONSUMPTION UNDER FREE ACCESS

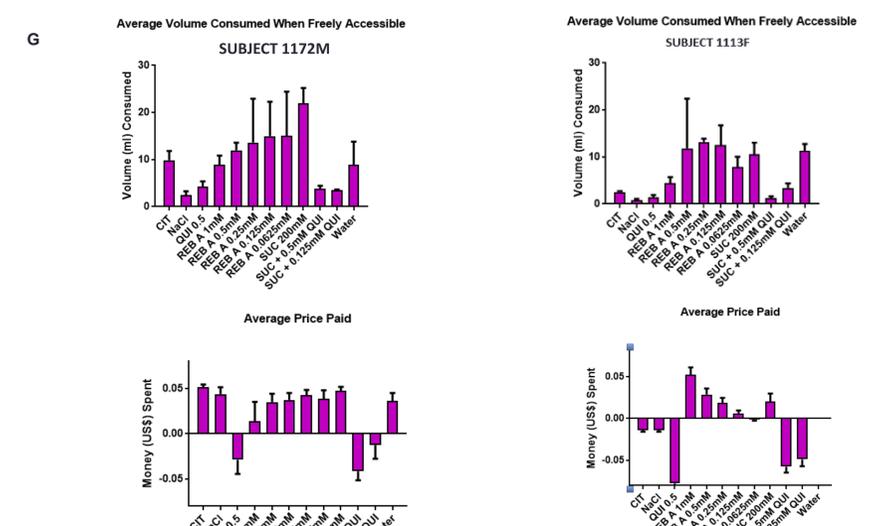
The solutions described in Figure C were dispensed as 30 ml volumes each in three of 36 plastic cups. The filled cups then were arranged in a randomized order on a table top. The subject was given a small paper straw to draw by mouth the solutions from the cups. At the start of the session, the investigator handed the first cup from the arrangement to the subject who was given the instruction to drink through the straw as much of the 30 ml as desired within 10 seconds (the 10-second timer was started when the subject had securely grasped the cup.) When the subject was finished drinking from the sample, the cup was handed back to the investigator, completing the trial. Each successive trial began when the subject indicated that they were ready (there was no set inter-trial interval). All subjects completed the task of drinking from all 36 cups in 15 minutes or less.



(E) Average price paid on each trial of a given sample to execute the action of “include” or “exclude” in the creation of a customized plate of taste stimulus solutions most “liked” by subjects 1172M and 1099F using the TaStation consumption model game; each of 12 solutions (“Plate A,” described in Figure C) was presented automatically and randomly in replicates of 8. Positive values on the ordinate indicate the absolute amounts of money spent for inclusion, whereas negative values indicate the absolute amounts of money spent for exclusion.

(F) Average volumes (out of 30 ml per sample) consumed through a straw by subject 1172M when given free access to the samples randomly presented in plastic cups; each of the 12 “Plate A” solutions was dispensed in 3 cups (i.e., total of 36 samples); the cups were given to the subject by the investigator in a randomized order. The dashed line highlights the average volume per sample of water consumed. CIT=citric acid (10 mM), NaCl=sodium chloride (100 mM), QUI=quinine, SUC=sucrose. Date shown in (A) and (B) were collected on separate days.

## INDIVIDUAL DIFFERENCES: OFF-TASTE SENSITIVITY



(G) Comparison between two subjects with differences in sensitivity to the off-tastes of Rebaudioside A. Subject 1113F is sensitive to the bittersweet off-tastes of the sweetener while subject 1172M is not.

## CONCLUSIONS AND FUTURE DIRECTIONS:

- The actual money spent by a subject on a tastant solution is a quantification of value
- The value in money assigned to the tastant solutions, which are freely available commodities, must be amplified by the expectation of return on investment by the virtual market.
- The overall pattern of spending predicts pattern of actual consumption.
- Magnitudes of actual expenditures vary across subjects, whereas actual volumes consumed appear to vary less.
- Variables that can be manipulated to enhance assay performance: a) starting amount in the pot b) incremental multiplier that reflects increasing value of each dollar spent as pot diminishes c) the virtual market