Impact of hedonic value of stimuli on sampling dynamics during a preference test

Ben Ballintyn, John Ksander, Donald Katz, and Paul Miller

Brandeis University

Abstract

The decision of whether to continue with a current action or to stop and consider alternatives is ever present in the life of an animal. Such continuous-time decision making lies at the heart of food preference tests whose outcomes are typically quantified by a single variable, the total amount consumed. However, the dynamics that give rise to such a quantity in terms of durations of bouts of sampling at a stimulus before pauses, and the impact of alternative stimuli on those bout durations and subsequent actions following a pause, can contain a richness of behavior that is not captured in a single palatability measure. Here we carry out multiple analyses of these dynamics, with a particular focus on assessing how the hedonic value of one taste stimulus impacts the behavior of a rat sampling a second taste stimulus during a preference test. We find evidence for an explicit competitive interaction between bout durations, such that the more palatable a stimulus the longer the bout durations when the rat samples the stimulus and the shorter the bout durations at the alternative. Such competition is reproduced in a model of a neural circuit that could underlie the continuous decision of when to end a sampling bout. We find that the competitive impact on bout durations is relatively short-lived whereas a competitive impact on the choice of which stimulus to approach following a pause persists. Such a discrepancy in the timescales for the decay of the impact of the alternative stimulus suggests different neural processes are involved in the choice of which stimulus to approach versus the choice of how long to sample from it. Since these two choices together combine to determine net consumption and therefore the inferred palatability or preference of a gustatory stimulus, our results suggest that palatability is not a unitary quantity but the result of at least two distinct, context-dependent neural processes.

Introduction

The ability to efficiently forage for food and other resources is critical to most animals' survival, and evolution has doubtless shaped the neural circuitry responsible for decision-making to optimize this task (Hayden et al., 2011; Pearson et al., 2014). There are many types of questions that an animal must answer during a foraging bout. A first class of questions lies within the domain of perceptual decision-making, where an animal uses its senses to gather information about the state of the environment to answer questions such as "is there a predator present?". A second class of problems constitutes value-based decision-making which uses available information to choose between different action plans such as "Is it worth continuing to gather food here, or should I search for a more abundant area?".

Studies of value-based decision-making have typically fallen into two categories: 1) "self-control" or "delay-discounting" tasks where animals tradeoff waiting times and payoff sizes (Bateson & Kacelnik, 1996; Blanchard et al., 2013; Pearson et al., 2010; Stephens, 2002; Stephens & Anderson, 2001) and 2) "stay-switch" or "patch-leaving" task where animals are presented with a source of reward and must decide when to leave it in search of a better alternative (Barack et al., 2017; Blanchard & Hayden, 2014; Constantino & Daw, 2015; Hayden et al., 2011). Patch-leaving tasks better represent the natural situation where animals have sequential interactions with individual reward sources as opposed to the simultaneous presentation of (cued) alternatives. While these prior patch-leaving studies have helped elucidate the neural circuits responsible for foraging behavior, they ubiquitously utilize a trial-based structure and patch options are presented randomly, as assumed by the Marginal Value

Theorem (Charnov, 1976), as opposed to in the wild, where animals use their experience with the environment to direct their encounters with patches. We suggest that two- or multi-bottle preference tests represent a simplified naturalistic foraging scenario where an animal can rapidly learn about the state of its environment and direct its encounters with reward options.

Preference tests are used widely to measure the relative hedonic values (or palatabilities) of a set of stimuli, with the degree of preference based on the amount of interaction the subject has with each stimulus. For example, in taste preference tests, the relative palatabilities of pairs of substances are measured by the total amounts consumed or the number of licks at each food source. It is assumed that the decision of the animal to lick (or eat) more of one tastant than another, given equal opportunity for time with both, reflects an underlying preference. While these tests have been used to determine the relative preferences of different options, little attention has been paid to the decision dynamics of animals during such preference tests. The lack of data quantifying the underlying behaviors that lead to the overall preference precludes the assessment of models of this type of decision-making. Indeed, one of the goals of our analyses is to test predictions of our recent modeling paper (Ksander et al., 2021).

Several questions can be asked about the sequences of decisions that animals make during these preference tests. Perhaps the most obvious and important is: Do animals rapidly settle on a favorite option or continue to switch between and sample both options? If the animal has a clear preference between two options (as revealed by the total amount consumed), then an intuitive and theoretically optimal strategy is to first sample both options to determine a

favorite and then spend all of the remaining time sampling the favored option (or until the source is exhausted or the animal is sated). In this case, it would be very difficult to quantify the palatability of a tastant: only a ranking would be possible. If the answer to the above question is "no" (as we find in our data), then several additional questions can be asked.

The first is, given that the animals switch back and forth between the two options, how do sampling times at one option depend on that option's palatability—as measured by total amount consumed in sessions without alternatives—and on the palatability of the alternative? To answer this question, we analyze durations of bouts of licking, which are comprised of series of rapid licks without significant pauses, to assess whether and how the behavior at one lick-spout depends on the contents of the alternative lick-spout.

Separate bouts are demarcated by pauses, following which the animal can either return to a new bout of licking at the same spout or switch to the alternative spout. Our analyses of bout durations separately following returns versus switches provides an indication of how the influence of the alternative sample on current behavior decays over time. Lastly, an analysis of the choice of which spout to choose after each pause, provides an insight into how the animal weighs the relative value of the two spouts. Distinct dynamics of that choice probability would provide evidence that the choice of which sample to taste and the choice of for how long to taste it are separate and distinct processes.

It is worth noting that competition arises in preference tests without the need for any direct interaction between the hedonic value of one alternative and the behavior displayed at the other. The source of implicit competition is the limited time available in most tasks, or even if time were not limited in a food preference test, the total amount of food desired until satiety provides a limit. Such limits mean that the more time spent and the greater the consumption at one sampled stimulus, the less time available at the alternative, even if the behavioral dynamics were not altered. Indeed, one can hypothesize that an association with a more appetizing stimulus might boost the perceived hedonic value of a paired neutral stimulus leading to longer bouts at the neutral alternative, even as total amount consumed at the neutral alternative goes down due to the fewer visits there. On the contrary, if behavior in preference tests resembles that during foraging, one would anticipate that the greater the value of the alternatives, the less time spent at a particular source. A primary goal of this work is to identify the nature of the across-stimulus interaction.

To summarize, we analyze the behavior of rats engaged in a naturalistic continuous-time taste preference task. We also compare the behavioral dynamics with the dynamics of a simulated circuit of model spiking neurons designed to possess two states, one representing the ongoing choice to sample a stimulus, the other to leave that stimulus. Competition between successive stimuli can arise in the model from adaptation-like processes, leading to predictions of a competitive interaction between one bout of sampling a stimulus and the subsequent bout with the alternative stimulus. We assess our behavioral findings for evidence of such a competitive interaction.

Results

Measurement of palatability

To study stay-switch decision dynamics, rats were put through two weeks of preference testing (Figure 1A/B). On each day, they were given one hour to freely sample a random two solutions drawn (with replacement) from a possible four (0M, 0.01M, 0.1M, or 1M) NaCl solutions, selected to provide three significantly different palatabilities (Sadacca et al., 2012). Licks at each solution spout were recorded using a custom circuit and identified using a semi-automated process (see methods).

As a first look at the rats' preference behavior, we confirmed the rank order of the relative palatabilities of these solutions (Figure 2A), by measuring the total number of licks to each solution on days where the solution was paired with itself and dividing by the mean number of licks to dH2O on dH2O only days. The previously determined palatability ranking (0.1M > 0.01M > 1M,(Sadacca et al., 2012)) was recapitulated, and no sex-specific differences were found (0.01M: $z = .17$, $p = .86$; 0.1M: $z = -1.056$ $p = .29$; 1M: $z = .51$, $p = .61$); data from both sexes were combined for all analyses in which different solutions were pitted against one another (see Methods and Figure 1).

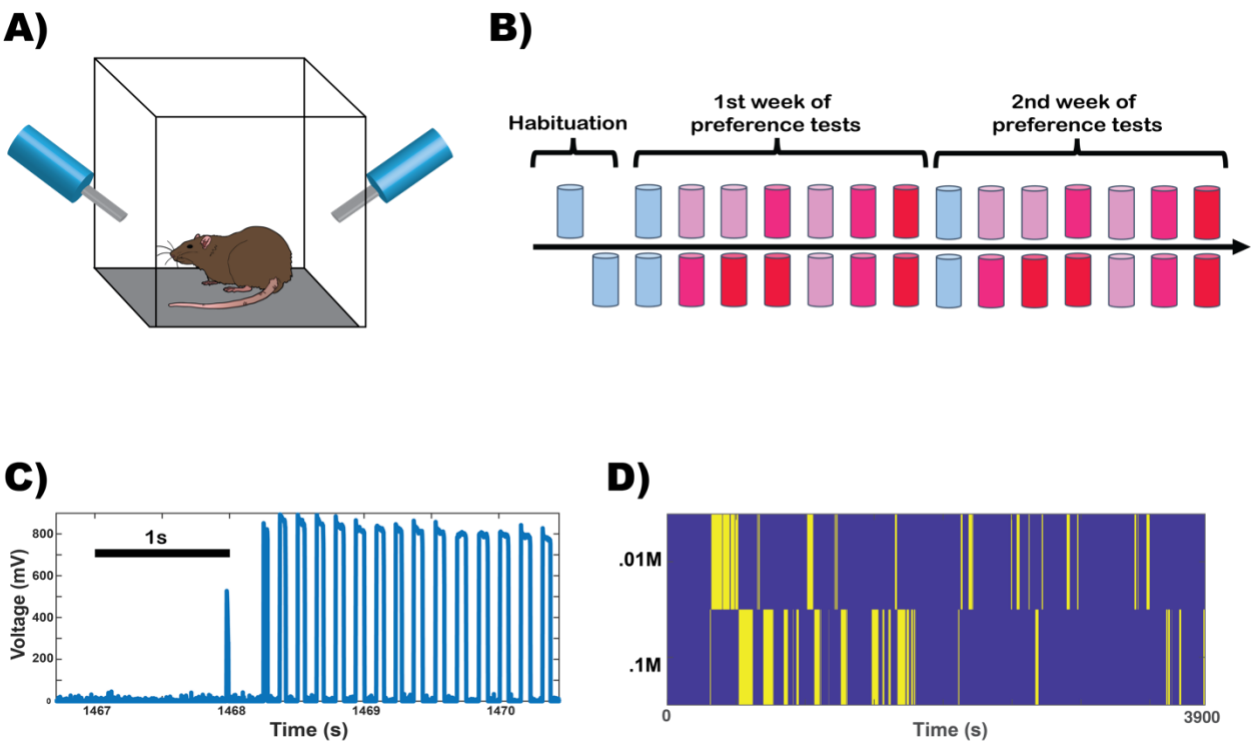

Figure 1. Behavioral setup and example behavior. ***A)*** *1' x 1' custom acrylic chamber had a solution spout available through the left and right walls each containing 25mL of 1 of 3 different NaCl solutions (0.01M, 0.1M, 1M) or dH2O. Rats were allowed to freely move and sample from either spout over the course of 1 hour.* ***B)*** *Preference test timeline. Rats were given 2 habituation days with 1 bottle of dH2O on opposite sides across sessions. This was followed by 2 weeks of sessions where each week started with a session of dH2O only followed by all 6 combinations of NaCl solutions.* ***C)*** *Example licking data. Each rectangular deflection is one lick. D) Example sampling data from a session with 0.01M and 0.1M NaCl solutions. Yellow stripes represent active sampling at the corresponding solution.*

Given the observed differences in palatabilities, we expected different distributions of sampling durations, with more palatable solutions having on average longer durations of lick bouts. This expectation was borne out: the distributions of bout durations of all solutions were well approximated by exponential distributions (Figure 2C-E), with decay constants akin to the mean time of bouts at each solution; these bout duration distributions are mostly commensurate

with the calculated palatability of each solution (dH2O: mean 13.39 ± .79s, .01M: mean 24.33 ± 1.69s, .1M: mean 27.54 ± 1.72s, 1M: mean 4.72 ± .29s).

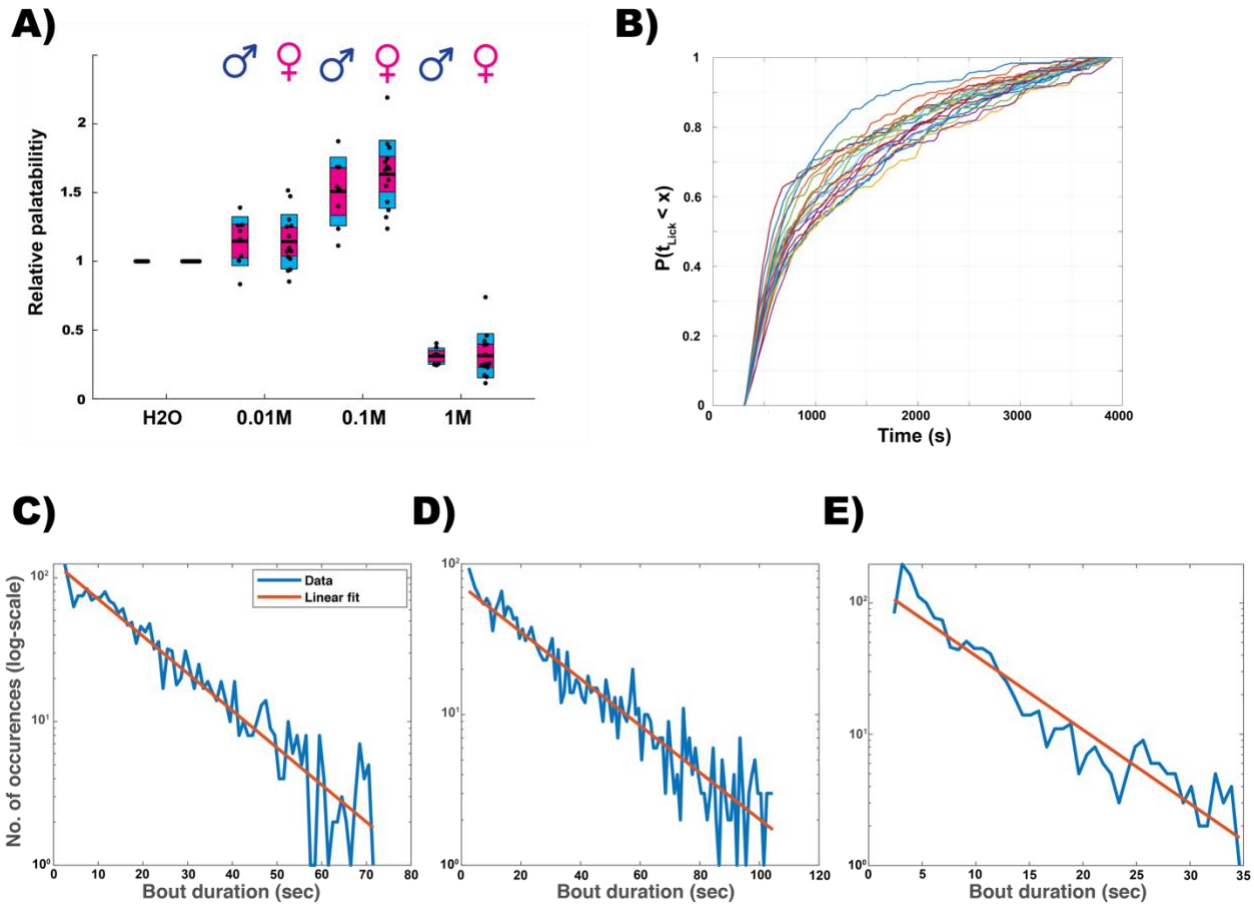

Figure 2. Effect of palatabilities on bout duration. ***A)*** *Relative palatabilities of the 3 NaCl solutions relative to water. Palatabilities are based on the total number of licks at each solution during sessions where the solution was paired with itself. No sex specific differences were found (0.01M: two-tailed: z = .17, p = .86,* ***.1M:*** *z = -1.06, p = .29,* ***1M:*** *z = .51, p = .61). Based on pairwise comparisons (the rank order of palatabilities from highest to lowest is (0.1M, 0.01M, H2O, 1M).* ***B)*** *Cumulative distribution of lick times. Rats continue to lick throughout the session but less over time. These CDFs were used to distinguish early and late bouts for each rat.* ***C)*** *Bout duration distributions were fit well by exponential distributions. Frequency of each bout duration for 0.01M NaCl with y-axis on a log-scale. Linear fits to the exponential data are shown in orange.* ***D)*** *Same as (C) but for bouts at the 0.1M solution.* ***E)*** *Same as (C,D) but for bouts at the 1M solution.*

Impact of relative palatability on bout duration

While a higher palatability of the currently sampled solution translates into longer sampling bouts, a critical unanswered question is how the palatability of the alternative solution in a preference test impacts these sampling bout durations. We considered three possibilities: 1) a high alternative palatability will have an appetitive effect, increasing the perceived palatability of the current solution and leading to longer sampling bouts; 2) conversely, a higher alternative palatability could reduce the perceived palatability of the current solution, leading to shorter sampling bouts; and 3) the palatabilities of alternative choices could have no impact on bouts at the current solution. Implied in hypotheses 1 or 2 is the maintenance of a memory of the alternative solution's value (palatability).

To evaluate the above possibilities we performed multilinear regression, predicting bout duration as a function of the palatability of available alternatives. As suggested by differences in mean bout durations across solutions, regression coefficients for the current solution's palatability were significantly positive ($z = 4.09$, $p = 2.15e-5$, mean = 15.78 ± 1.63) – that is, the more palatable a stimulus the longer the bouts of licking at it (Fig. 3A). Alternative palatability coefficients were found to be significantly negative (mean -5.69 ± 1.32), consistent with possibility 2 above (Fig. 3B)—durations of bouts are shorter when the alternative stimulus is of higher palatability.

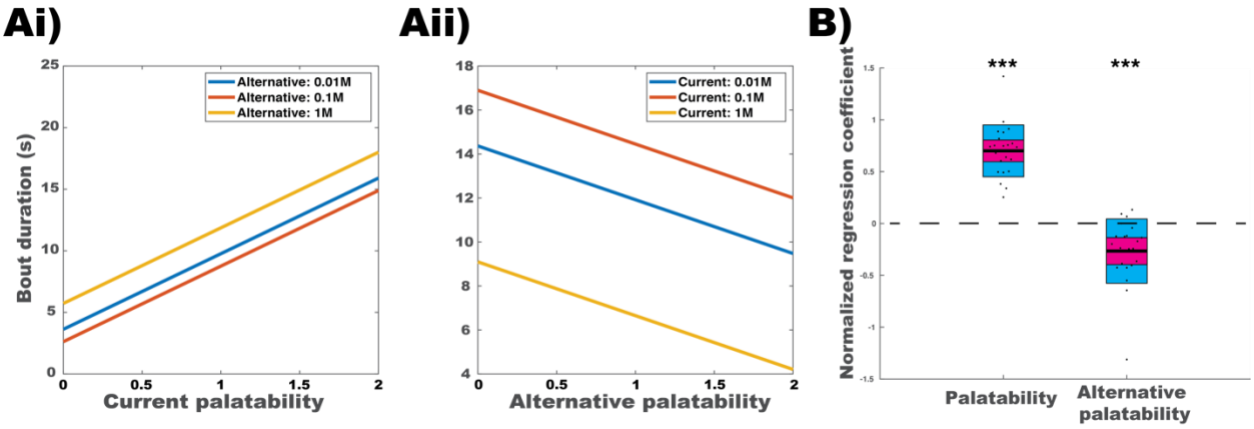

Figure 3. Effect of current/alternative palatability on duration of lick bouts. ***A)*** *Example results from 1 rat of a multilinear regression model for predicting bout duration with the currently sampled solution's and alternative solution's palatabilities as factors.* ***Ai)*** *Using best fit regression coefficients for 1 rat, bout duration is plotted against the current solution's palatability for all 3 possible alternative solutions.* ***Aii)*** *Same as (Ai) but plotting bout duration vs. the alternative solution's palatability for 2 levels of the current solution's palatability.* ***B)*** *Current and alternative palatability regression coefficients normalized by the mean bout duration for each rat. Normalized coefficients for current palatability are significantly positive (right-tailed: z = 4.09, p = 2.15e-5) and those for alternative palatability are significantly negative (left-tailed: z = -3.57, p = 1.7e-4).*

The above results were stable across the course of the session, even though bout durations in general decreased over time (likely due to satiation). When we split sessions into 'early' and 'late' portions based on a per-animal criterion (we used the 2nd derivatives of each rat's cumulative distribution of lick times to detect the "kink" in the curve of Fig. 2B, where licking slowed from a high rate to a lower rate) and performed the same multilinear regression on early/late bouts separately, we found no significant change in (normalized) regression coefficients between the early and late portions of the session (Fig. 4A/B).

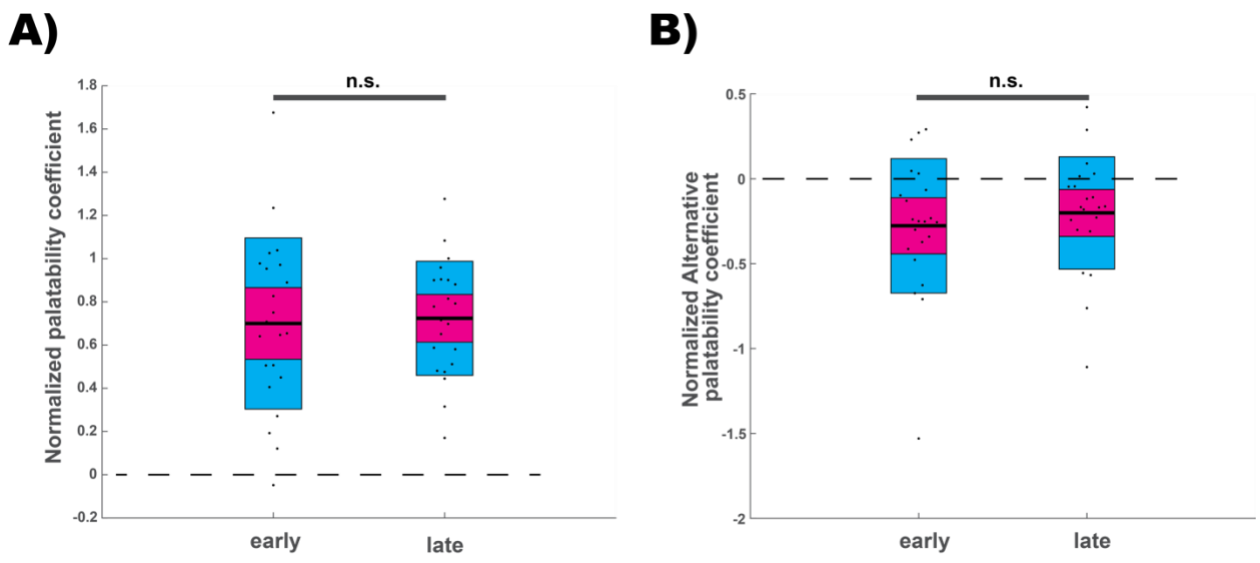

Figure 4. Effect of palatability on bout duration is constant across early and late portions of the session. ***A)*** *Normalized regression coefficients for current solution palatability for bouts in the early or late portion of the session. Current palatability coefficients were significantly positive for both the early (right-tailed: z = 4.06, p = 2.47e-5) and late (right-tailed: z = 4.09, p = 2.15e-5) portions of the task. Coefficients were not significantly different across portions of the session (paired: z = -.11, p = .91).* ***B)*** *Same as (A) but for the alternative solution's palatability. Normalized coefficients were significantly negative for both early (left-tailed: z = -2.99, p = 1.4e-3) and late portions of the session (left-tailed: z = -2.76, p = 2.9e-3). Coefficients were not significantly different across portions of the session (paired: z = -.76, p = .45).*

We next split bouts into those following stay or switch decisions to ascertain whether the same decision process was at play for each type of decision. We again repeated the multilinear regression analysis on these groups individually. We found that regression coefficients for current palatability are similarly positive following stays (z = 4.09, p = 2.15e-5, mean = 15.46 $\pm$ 1.93) and switches (z = 4.06, p = 2.4e-5, mean = 16.04 $\pm$ 2.38), with no significant difference between the two groups (z = .011, p = .91, Fig. 5A). In contrast, there is a significant difference in alternative palatability coefficients in the post-stay vs. post-switch bouts: coefficients for the post-switch bouts were significantly more negative (z = 4.06, p = 2.4e-5) than those following a stay decision, which were themselves not significantly different from zero (z = -1.7, p = .088,

mean = -1.09 ± 1.61, Fig. 5B). This result suggests that information regarding the alternative solution may only factor into decisions about sampling times only following a switch between the two samples.

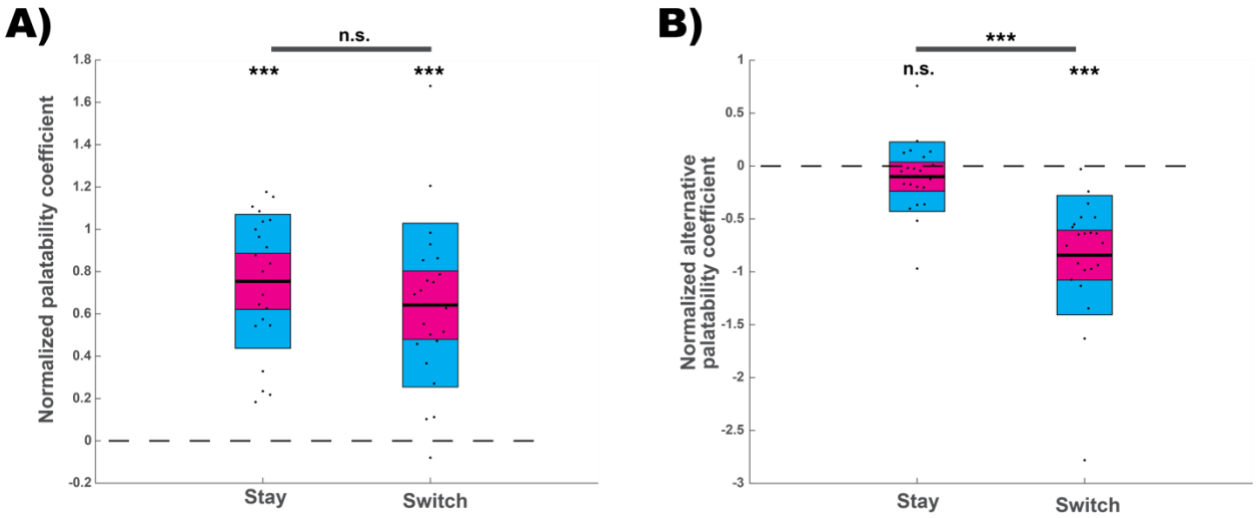

Figure 5. Difference in impact of current/alternative palatability on bout duration following a stay or switch decision. ***A)*** *Normalized multilinear regression coefficients for the currently sampled solution's palatability are significantly positive following both a stay (right-tailed: z = 4.09, p = 2.1e-5) and switch decision (right-tailed: z = 4.06, p = 2.4e-5). Coefficients were not significantly different across stay/switch conditions (paired: z = .011, p = .91).* ***B)*** *Normalized multilinear regression coefficients for the alternative solution's palatability are not significantly different from zero following a stay decision (two-tailed: z = -1.7, p = .088) but are significantly negative for bouts following a switch decision (left-tailed: z = -4.09, p = 2.1e-5). Coefficients for bouts following a switch decision are significantly more negative than those for bouts following a stay decision (paired right-tailed: z = 4.06, p = 2.5e-5).*

Lack of dependence of results on bout definition criteria

For the analyses described above, we define a 'licking bout' as sequences of licks which had no period of >2s of no contact with the lick spout. Here, 'contact' includes brief periods of nose-poking at the spout. While this definition of a 'licking bout' slightly overestimates the total time spent licking, brief periods of nose poking in between licks represent active engagement with

the spout rather than a decision to stop sampling or switch to the alternative. An inter-lick-interval of 2s was used as rats never switched between solutions in <2s.

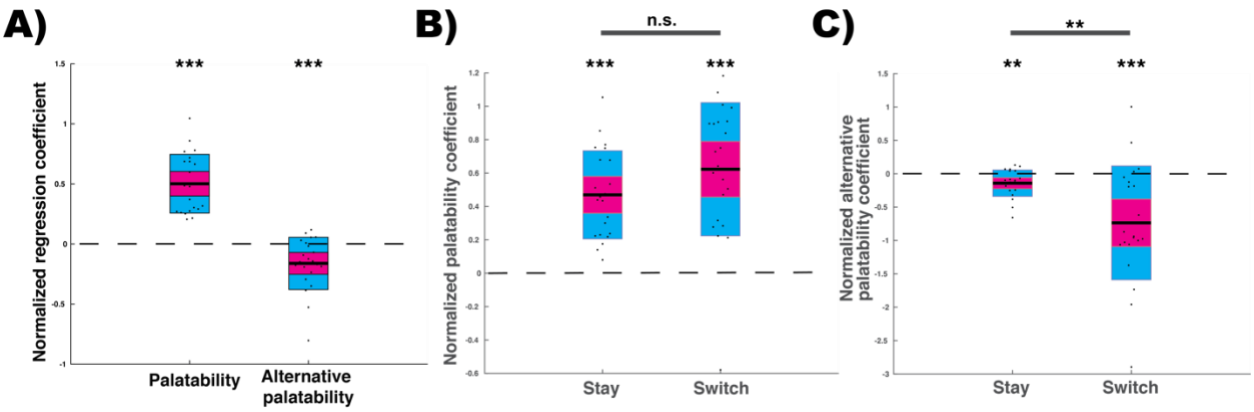

Figure 6. Using a 200ms ILI interval criterion to define bouts does not significantly alter the results. ***A)*** *As in Fig 3B, normalized multilinear regression coefficients for predicting bout duration using the currently sampled and alternative solutions' palatabilities as factors are shown. Current palatability coefficients were significantly positive (right-tailed: z = 4.09, p = 2.1e-5) and alternative palatability coefficients were significantly negative (left-tailed: z = -3.15, p = 8.2e-4).* ***B)*** *As in Fig 5A, normalized multilinear regression coefficients for the currently sampled solution's palatability are significantly positive following both a stay (right-tailed: z = 4.09, p = 2.1e-5) and switch decision (right-tailed: z = 3.8, p = 7.3e-5). Coefficients were not significantly different across stay/switch conditions (paired two-tailed: z = -1.7, p = .089).* ***C)*** *Multilinear regression coefficients for the alternative solution's palatability are shown for models predicting bout durations following a stay or switch decision. Using this criterion, regression coefficients for bouts following a stay decision are significantly negative (left-tailed: z = -3.08, p = .001) and following a switch decision (left-tailed: z = -3.25, p = 5.8e-4). Coefficients for bouts following a switch decision are significantly more negative than those for bouts following a stay decision (paired right-tailed: z = 2.82, p = .0024).*

Of course, this is only one dividing line that could be used. Prior studies of licking microstructure in rats (Davis, 1996; Davis & Smith, 1992) have grouped licks into 'bursts' or 'clusters' based on a <250ms or >500ms inter-lick-interval (ILI) criterion. To test that the results presented above are not artifacts of our choice of bout definition, we repeated all the above analyses using a 200ms ILI criterion. In this re-analysis, the magnitudes of the resulting

264 regression coefficients are much smaller, since bout lengths themselves are much shorter
265 (Supp. Fig. 1). Nonetheless, all the qualitative results presented above hold (Figs. 6/7):
266 coefficients for current palatability are significantly positive for early vs. late and stay vs. switch
267 bouts, and coefficients for alternative palatability in early and late bouts do not differ; while
268 coefficients for alternative palatability are significantly negative following a stay decision using
269 this bout criterion ($z = -3.02$, $p = .0012$, mean = $-.61 \pm .19$), they are again significantly more
270 negative (mean = $-2.6 \pm .68$) following a switch decision ($z = 2.59$, $p = .0047$).
271
272 One interesting difference did arise with this more stringent bout length criterion, as revealed
273 in Figure 6C compared with Figure 5B. The more stringent criterion split many prior single bouts
274 into multiple bouts of shorter duration. The shorter duration of bouts meant that the time
275 passed from a sampling of the alternative stimulus would often be less than previously for a
276 repeated bout of sampling at a stimulus – that is a bout of sampling following a "Stay" decision.
277 As a result, in Figure 6C we see a small significant impact of the alternative stimulus following a
278 "Stay" decision that was absent in Figure 5B where bout durations were longer. Such a finding
279 is consistent with a model in which the impact of the alternative stimulus on a current bout's
280 duration decays gradually over a period of many seconds after leaving that stimulus.
281
282 ***Indifference of results to change in rank order of palatability***
283 As noted above, we calculated palatabilities using data from days in which identical solutions
284 were available at both spouts (this was done to separate the data used to compute
285 palatabilities from those used in the multilinear regressions). Using this method, 0.1M NaCl was

found to be significantly more palatable than 0.01M (Figure 2A). However, on days in which 0.1M NaCl was paired with 0.01M, rats licked more—on average, 1.3x as much—for 0.01M than 0.1M. That is, the 0.01M solution seemed more palatable than the 0.1M solution in direct comparisons.

To the best of our knowledge, this is the first time a study has compared palatabilities obtained by comparison to water and through direct comparison. This difference might be explained by an appetitive effect whereby the palatability of the 0.1M is reduced when paired with the less palatable 0.01M with the converse being true for the 0.01M (made more palatable by pairing with 0.1M). Alternatively, these differences could simply represent the inherently context-dependent nature of palatability.

In either case, we tested whether our prior results were impacted when the palatability of the 0.01M solution was defined as a factor of 1.3 times greater than that of the 0.1M solution. We find that the results for the alternative palatability regression coefficients do not change. That is, in aggregate, coefficients for alternative palatability are significantly negative ($z = -3.3$, $p = 4.5e-4$, mean = -5.69 ± 1.32, Fig. 7A), coefficients for bouts following a switch decision were significantly more negative than for those following a stay decision ($z = 4.09$, $p = 2.15e-5$, Fig. 7C), and coefficients were not significantly different between early and late portions of the session ($z = -.5$, $p = .61$, Supp Fig. 2B). That is, our qualitative results are robust to whether the 0.01M or 0.1M solution is the more palatable and all conclusions arise from those two solutions being more palatable than the 1M NaCl solution.

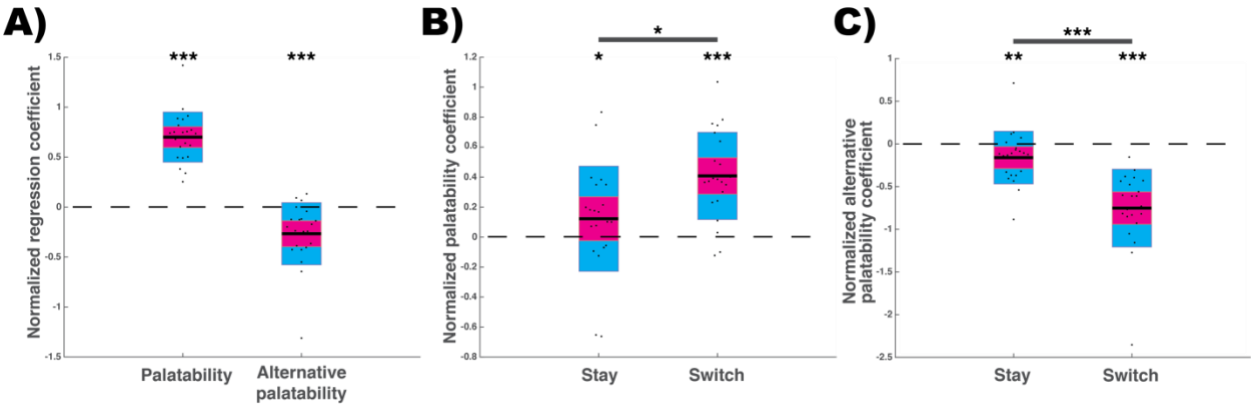

Figure 7. Impact of current/alternative palatability on bout duration when artificially setting Palatability(.01M) = 1.3 x Palatability(.1M). ***A)*** *As in Fig 3B, multilinear regression coefficients for predicting bout duration using the currently sampled and alternative solutions' palatabilities as factors are shown. Current palatability coefficients were significantly positive (right-tailed: z = 4.09, p = 2.1e-5) and alternative palatability coefficients were significantly negative (left-tailed: z = -3.57, p = 1.7e-4).* ***B)*** *As in Fig 5A, multilinear regression coefficients for the currently sampled solution's palatability are significantly positive following both a stay (right-tailed: z = 2.17, p = .0148) and switch decision (right-tailed: z = 3.9, p = 4.9e-5). With these artificially altered palatabilities, the coefficients for bouts following a switch decision were significantly more positive than those for bouts following a stay decision (paired left-tailed: z = -2.2, p = .014).* ***C)*** *As in Fig 5B, multilinear regression coefficients for the alternative solution's palatability are shown for models predicting bout durations following a stay or switch decision. With the artificially altered palatabilities, regression coefficients for bouts following a stay decision (left-tailed: z = -2.56, p = .0052) and following a switch decision (left-tailed: z = -4.09, p = 2.15e-5) are significantly negative. Coefficients for bouts following a switch decision are significantly more negative than those for bouts following a stay decision (paired right-tailed: z = 4.09, p = 2.15e-5).*

There are however some minor differences regarding the coefficients for current palatability. Coefficients for current palatability are significantly more positive following a switch decision (z = -3.05, p = .0011, Fig. 8B) and normalized regression coefficients in the late portion of the session were significantly smaller (less positive) than those in the early portion of the session (z = 3.18, p = 7.3e-4).

Impact of palatability on transition probability

Thus far, our results describe sampling duration as a function of the palatabilities of the two solutions. To fully understand the impact of palatability on choice dynamics, we also asked whether the palatability of the current or alternative solution impacted the transition probabilities between the solutions. A transition could be from a solution back to the same solution, if following a bout of licking there is a pause then a return to the same solution. Therefore, we are assessing the degree to which, following a pause in licking, the rat returns to the same solution or switches to the alternative. As with measurements of bout durations, the choice to return or switch could depend on both the palatability of the most recently sampled ("current") solution and that of the alternative.

To dissociate the contributing factors, we compared the transition probabilities between pairs of solutions with either a common source (e.g. 0.01M -> 0.1M and 0.01M -> 1M) or a common target (e.g. 0.01M -> 0.1M and 1M -> 0.1M). If the palatability of the current solution was to influence transition probability, this influence would be reflected in a higher probability of switching to a common target taste from a taste with a low palatability than from a taste with a high palatability. Similarly, if alternative palatability was to impact transition probability, this would be reflected in a higher probability of switching from a common source to a solution with high palatability.

We find evidence that palatability of both the current and the alternative solution impacts the transition probabilities (Fig. 8A-B). These results are further supported by a logistic regression

model trained to predict switches based on the current and alternative palatability. In the regression model, both current palatability ($p = 4.89e-31$, coefficient = -.948, 95% CI = [-1.1 -.78]) and alternative palatability ($p = 3.15e-21$, coefficient = .63, 95% CI = [.5 .76]) are found to be significant factors.

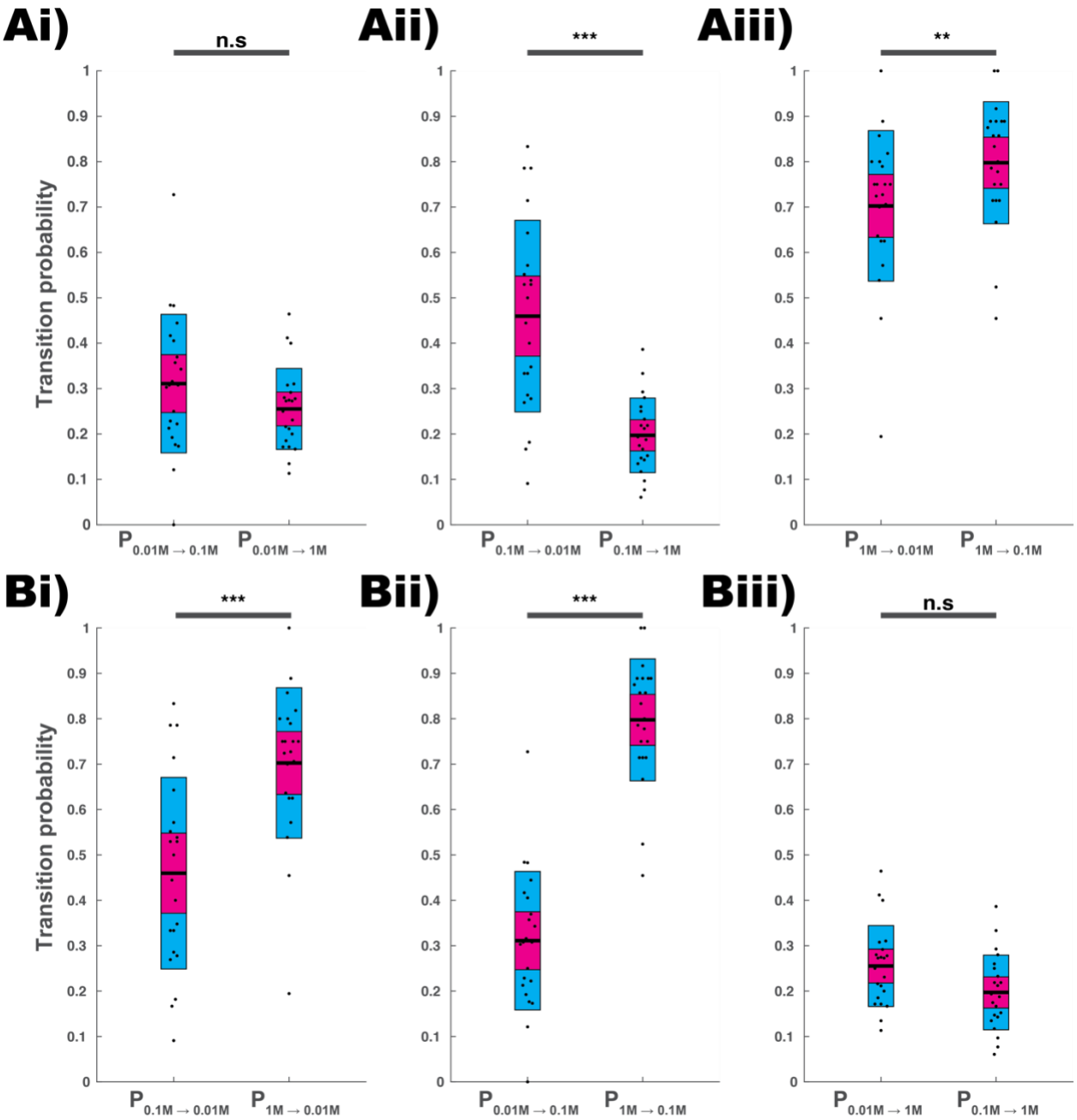

Figure 8. Comparison of transition probabilities for transitions with a common source/target. ***A)*** *Transition probabilities for transitions with a common source (0.01M -> 0.1M and 0.01M -> 1M, 0.1M -> 0.01M and 0.1M -> 1M, 1M -> 0.01M and 1M -> 0.1M) reveal the influence of a memory of the alternative solution's palatability.* ***Ai)*** *P(0.01M -> 0.1M) and P(0.01M -> 1M) are not significantly different (paired two-tailed: z = 1.51, p = .13).* ***Aii)*** *P(0.1M -> 0.01M) is significantly higher than P(0.1M -> 1M) (paired right-tailed: z = 3.73, p = 9.4e-5).* ***Aiii)*** *P(1M -> 0.01M) is significantly lower than P(1M -> 0.1M) (paired left-tailed: z = -2.52, p = 5.8e-3).* ***B)*** *Transition probabilities for transitions with a common target (0.1M -> 0.01M and 1M -> 0.01M, 0.01M -> 0.1M and 1M -> 0.1M, 0.01M -> 1M and 0.1M -> 1M) reveal the influence of the last sampled solution's palatability on switch*

probability. ***Bi)*** *P(0.1M -> 0.01M) is significantly lower than P(1M -> 0.01M) (paired left-tailed: z = -3.63, p = 1.3e-4).* ***Bii)*** *P(0.01M -> 0.1M) is significantly lower than P(1M -> 0.1M) (paired left-tailed: z = -4.09, p = 2.15e-5).* ***Biii)*** *P(0.01M -> 1M) is significantly higher than P(0.1M -> 1M) (paired right-tailed: z = 2.43, p = 7.5e-3).*

No evidence for memory across days

Lastly, we investigated whether rats held a bias for the first side they visited in a session based on their experience the prior day. To do this, we counted the number of times rats first visited the side they preferred (had the most licks at) on the prior day and compared this to the number expected. Given a null hypothesis of no memory across days, the expected number is given by the binomial distribution with p = q = 0.5. Our results are consistent with the null hypothesis that rats did not carry a preference for side across days ($\hat{p} = .485, 95\%\ CI = [.424\ .547]$, Fig. 9).

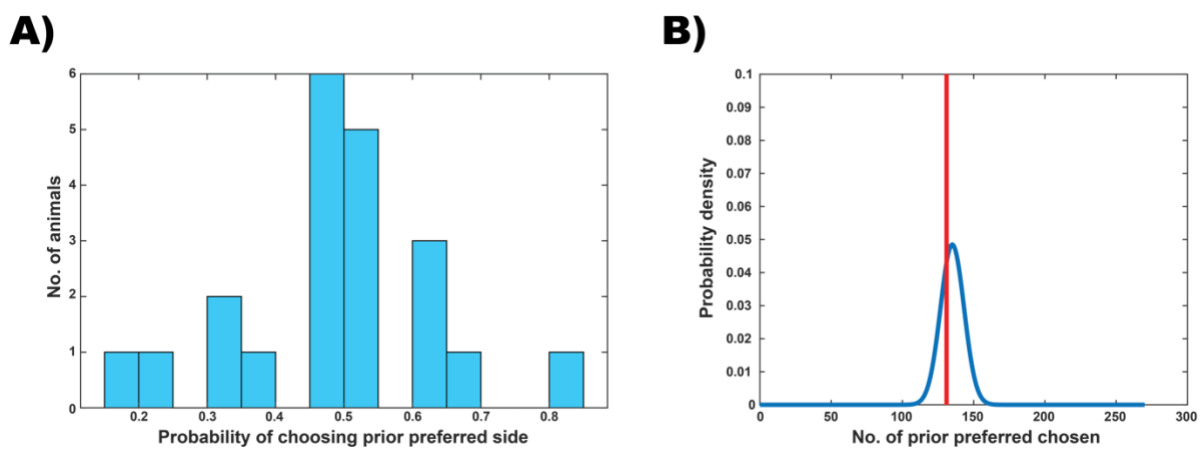

Figure 9. No evidence for preference across days. ***A)*** *Histogram showing the fraction of times rats first sampled from the side they preferred on the prior day.* ***B)*** *(blue) Probability density function for the total number of times (across all rats) that rats first sampled from the side they preferred on the prior day which is given by the binomial distribution with N = 270, p = q = 0.5. (red line) Total number of times rats first sampled from the preferred side from the prior day.*

Comparison to spiking network models

381 In our modeling study (Ksander et al., 2021) we found competition in the durations of an
382 activity state representing bout duration in response to alternating stimuli. The competition
383 arose from a slow synaptic depression in the model so we hypothesized that the competition
384 between successive stimuli would diminish over the timescale of recovery from that synaptic
385 depression. We predicted that the impact of the alternative stimulus on bout duration would,
386 therefore, be significantly lower, during a second or later successive bout at the same stimulus,
387 as compared to the first bout at that stimulus following a switch, just as seen in the behavioral
388 data (Figs. 5-7). Therefore, we adapted the stimulus protocol in our prior study such that
389 following any state transition indicating the end of a bout of sampling, the subsequent stimulus
390 presented was chosen randomly, with a 50% probability for each of the two stimuli being
391 compared in that preference test.

392 Our results are shown in Figure 10, in which we produced regression coefficients in the
393 same manner as Figs. 5-7 but based on the state durations arising from three preference tests
394 (the distinct pairs of three stimuli of different strengths, representing different palatability) for
395 each of two types of network. Figure 10A-C depicts the results of an “entice-to-stay” network in
396 which stimuli of greater palatability were modeled by increased excitatory stimulus to neurons
397 whose activity represented a “stay” state that enhanced bout duration. The results are
398 qualitatively identical to the behavioral data (Figs. 3 and 5-7) with the alternative stimulus
399 having a competitive impact on bout duration (a negative regression coefficient, Fig. 10A) but
400 with the impact diminished following a repeat bout (a “stay” transition, Fig. 10C) at the same
401 stimulus. On the other hand, the results of a “repel-to-leave” network shown (Fig. 10D-F) did
402 not match the behavioral data well. The asymmetry between the model networks arises

because only in the “entice-to-stay” network does greater stimulus input correspond to longer state durations, as needed to maximize the impact of synaptic depression.

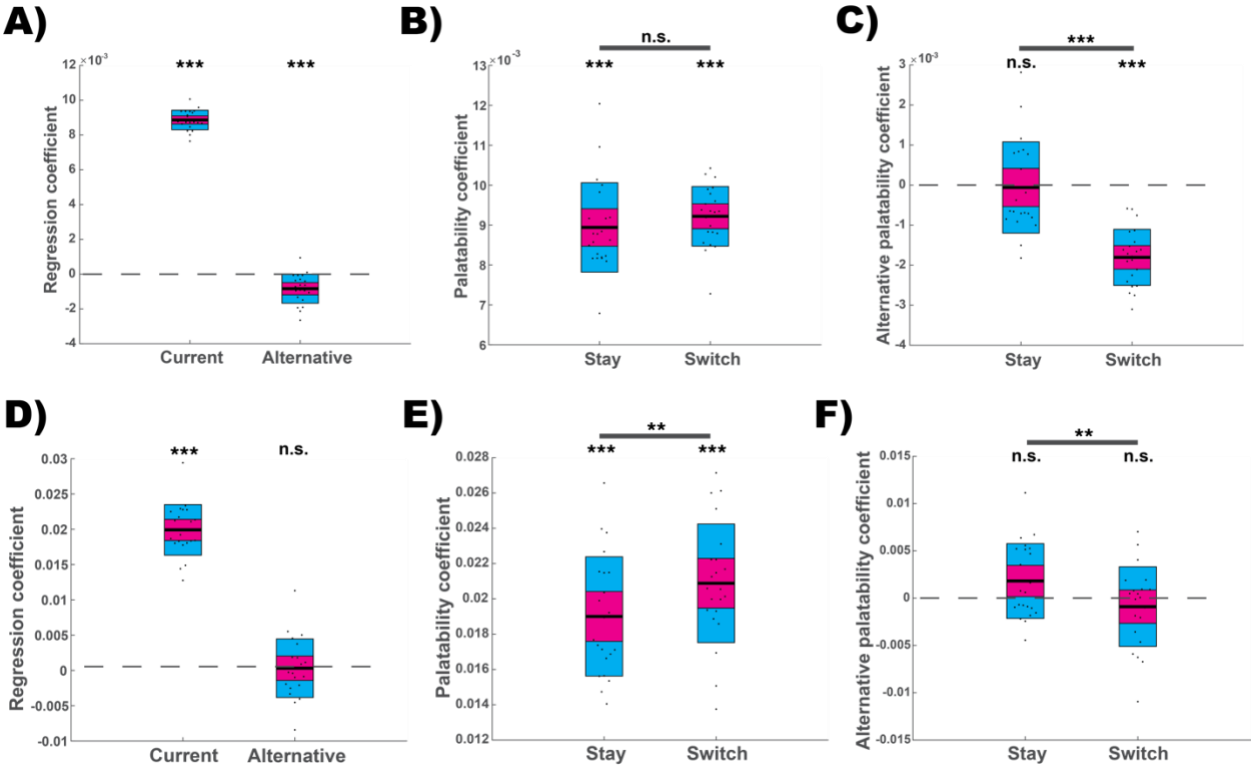

Figure 10. ‘Fast’ (‘entice-to-stay’) (A-C) but not ‘slow’ (‘repel-to-leave’) (D-F) model networks replicate rat behavior. ***A)*** *As in Fig. 3B regression coefficients for predicting bout duration as a function of current and alternative palatability are shown for ‘fast’ networks. Similar to rats, coefficients for current palatability are significantly positive (right-tailed: z = 4.09, p 2.15e-5) and coefficients for alternative palatability are significantly negative (left-tailed: z = -3.83, p = 6.38e-5).* ***B)*** *As for rats, palatability coefficients for both stay (right-tailed: z = 4.09, p = 2.15e-5) and switch (right-tailed: z = 4.09, p = 2.15e-5) bouts were significantly positive and are not significantly different between groups (paired two-tailed: z = -1.8, p = 0.07).* ***C)*** *As for rats, alternative palatability coefficients for bouts following a stay decision were not significantly different from zero (two-tailed: z = -1.28, p = 0.19) whereas coefficients for bouts following a switch decision are significantly negative (left-tailed: z = -4.06, p = 2.47e-5)).* ***D)*** *In contrast, ‘slow’ networks did not replicate the pattern of coefficients of rats. Coefficients for current palatability were significantly positive (right-tailed: z = 4.09, p = 2.15e-5) but those for alternative palatability were not significantly different from (two-tailed: z = 0.14, p = 0.88).* ***E)*** *Palatability coefficients following both stay (right-tailed: z = 4.09, p = 2.15e-5) and switch (right-tailed: z = 4.09, p = 2.15e-5) bouts were significantly positive and coefficients for switch bouts were significantly more positive than those for stay bouts (paired left-tailed: z = -2.53, p = 0.0057).* ***F)*** *Alternative palatability*

coefficients for both stay (two-tailed: $z = 1.57$, $p = .115$) and switch (two-tailed: $z = -0.73$, $p = 0.465$) bouts were not significantly different from 0. Alternative palatability coefficients for switch bouts were significantly lower than for stay bouts (paired right-tailed: $z = 2.89$, $p = 0.0019$).

Discussion

Palatability is typically measured as the amount of a food or solution consumed. The amount solution consumed by a rat, for example, is equal to the number of licks taken multiplied by the mean amount consumed per lick. Given that the mean amount consumed per lick has been shown to vary little across stimuli or time, we assume that is constant in this study and measure palatability as the number of licks of a solution. Since rats sample a solution in clearly demarcated bouts of high frequency (approximately 6 Hz) regular sampling, we can identify two distinct factors that impact the total number of licks and hence the palatability: the duration of the bouts and the total number of bouts. In theory, bout durations could be independent of a stimulus such that its palatability is only evident in the total number of bouts. However, prior work (Davis, 1996) has shown that the more palatable a stimulus, the longer the bouts, a result which we recapture here. In a more novel direction, we have assessed how, in a preference test, the palatability of one stimulus impacts the behavior of an animal at the alternative stimulus. Our main finding is that the more palatable one stimulus the shorter the bouts of licking at the alternative as compared to when that alternative is paired with a less palatable stimulus.

The second factor determining the number of licks at a spout is the total number of times the spout is visited. Therefore, we also analyzed the transition probability during preference tests,

441 which indicates that after a bout of sampling from one lick spout how likely is an animal to
442 return to the same lick spout or to transition to the alternative. We find that the likelihood to
443 return increases with the palatability of the stimulus just tasted. In of itself such behavior would
444 produce competition in the total amount consumed, as it would produce more repeated bouts
445 at sources of high palatability, leading to fewer at an alternative. However, we also found that
446 following a pause in sampling at one lick spout memory of the alternative also impacted the
447 likelihood to return to the same spout, such that the more palatable the alternative, the less
448 likely to return. Thus, the choice of which spout to lick from is impacted by memory, which has
449 persisted beyond a single bout's duration, of the contents of both lick spouts.
450
451 Our findings of the competitive interaction between stimuli on bout durations supports a
452 recent model (Ksander et al., 2021) in which the duration of a bout is given by the duration of a
453 particular state of activity in a neural circuit. In the model, noise fluctuations terminate states of
454 activity, leading to an exponential-like distribution of state durations, just as we find in the
455 behavioral data. Moreover, the impact of the well-established neural-circuit level process of
456 synaptic depression in the model leads to a competitive impact between successive stimuli,
457 such that following a highly palatable stimulus a subsequent bout duration is shorter than
458 otherwise expected. Since the underlying biological processes have a limited timescale, we
459 tested and found in the model that such a competitive impact on bout durations diminishes
460 over time and is much weaker for bouts following a return to a stimulus when the time passed
461 since the visit to the alternative has increased. Indeed, we find in our behavioral data a similar

462 fact, with no impact of the alternative stimulus on durations of bouts of sampling that do not
463 directly follow a switch from that alternative stimulus.
464
465 When a food substance or taste stimulus is considered palatable of unpalatable, the implicit
466 suggestion is that palatability is a property of a substance to be ingested. However, in practice,
467 palatability is a measure of behavior—typically the total amount of a substance consumed—so
468 is inherently dependent on the state of an animal and the context in which the animal is
469 sampling the stimulus. In our study we find that even the rank order of palatability can be
470 altered depending on context. When a rat has two lick spouts available to it, both of which
471 contain the same solution, in accordance with prior work (Sadacca et al., 2012) we find rats lick
472 the spouts more often when the solution is 0.1M NaCl than when the solution is 0.01M NaCl
473 (Fig 1). Such a finding suggests that 0.1M NaCl is more palatable to rats than is 0.01M NaCl.
474 However, when one lick spout contains 0.1M NaCl and the other contains 0.01M NaCl, we find
475 rats lick more often at the spout containing 0.01M NaCl, suggesting a switch in relative
476 palatability and preference of the two salt solutions in the new context. Such a switch is
477 intriguing and its cause warrants further investigation. Fortunately, our findings in this paper on
478 the interactions between stimuli were robust to the switch. That is, whether we assumed 0.1M
479 NaCl was more or less palatable than 0.01M NaCl did not alter the findings on how the
480 palatability of the alternative stimulus impacted the behavior at a lick spout.
481
482 Our findings of a competitive interaction of palatability of bout durations of alternatives and
483 our model of the process contribute to the foraging literature, in which behavior is discussed

historically in terms of the Marginal Value Theorem (Charnov, 1976). The theorem prescribes optimal behavior in an environment with multiple sources, at each of which the rate of reward diminishes with the time an animal spends at the source. Specifically, an animal should only stay at a food source until its rate of reward has depleted to the mean rate of reward it would achieve by moving from alternative source to alternative source and remaining the optimal time at the alternative sources. Our behavioral findings and model are in qualitative accordance with such behavior in that the more palatable an alternative (*i.e.,* the greater the mean rate of reward) the less time spent at a source while the reduction is ameliorated over time (the greater the time between sources in foraging, the lower the mean rate of reward, so time spent at a diminishing source increases). However, unlike in foraging studies, in preference tests the potential rate of reward at a lick spout is constant, so if one spout contains more rewarding solution than the other, the optimal behavior of an animal would be to stay at the more rewarding spout as soon as it has sampled both. That the animals do not behave in such a manner, but continue to sample even aversive stimuli many times, is either an indication of limited memory duration (*i.e.,* they forget what is in each spout) or a strong drive to explore in case the environment changes.

Acknowledgements

We are grateful for support from NIH (NIDA) NRSA grant DA051155 to BB, NIH (NINDS) grant NS104818 via the Brain Initiative to DBK and PM, and to the Swartz Foundation for support to

JK. Computational resources were provided by the Brandeis HPCC which is partially supported by the Brandeis Center for Bioinspired Soft Materials, an NSF MRSEC, DMR-2011846.

Methods

Behavioral apparatus

The preference test was carried out in 1’ x 1’ x 1’ custom acrylic chambers. Each chamber has 3 holes through which rats could lick a stainless steel solution spout. There is one hole on each of the left, right, and back walls of the chamber. For this study, only the left and right sides ever had a solution spout. In order to record licks, a custom circuit, based on a published design (Hayar et al., 2006) was used. A small voltage was applied to the stainless steel floor of the chamber such that when the rat licked one of the solution spouts, a voltage deflection (measuring the water-metal junction potential) was recorded. A RaspberryPi was used to both supply power to the floor and record licks using custom Python software.

Preference test

22 adult Long-Evans rats (14 female, 8 male) from Charles River were water deprived for 22 hours prior to the first habituation session. The preference test timeline consisted of 16 1 hour sessions of which the first 2 were habituation sessions with only 1 bottle of dH2O available on one side of the experimental chamber (the side was switched for the second habituation session). Following each session, rats were given 1 hour of ad lib access to water in their home cage such that they were deprived of water for 22 hours prior to each session. After the two

habituation days, the first day of the preference test was always a session with 2 bottles of dH2O. This was followed by 6 consecutive days of pairings of 3 NaCl concentrations (0.01M, 0.1M, 1M) including self pairings. This was then repeated for a second week such that each rat experienced 2 dH2O only sessions and 2 pairings of each combination of NaCl concentrations. These concentrations were used because they had been previously measured to have different palatabilities (Sadacca et al., 2012) covering both palatable and unpalatable (at least relative to water) tastants.

Lick identification

Licks were identified via a semi-automated process using custom MATLAB software. A simple threshold could not be used to identify licks because both licks and nose pokes were picked up as large voltage deflections. Additionally, occasionally a rat would maintain contact with the lick spout while licking resulting in a sustained voltage deflection on top of which licks could be seen. As a result, we produced a dataset of hand-identified licks from the data of the first few rats and used MATLAB's neural network toolbox to train a bidirectional LSTM recurrent neural network to predict the presence or absence of a lick at any point in time. These automatic identifiers were then used as a first pass on all future data to capture presumptive licks, which were then accepted/discarded by eye based on the stereotypical shape and timing of licks. Lastly, a final pass over the data was made by eye to ensure that no licks were missed by the neural network.

Lick bout identification

548 Following identification, licks were grouped together into 'bouts' based on 3 different inter-lick
549 interval (ILI) criteria. That is, we repeated all analyses described below using bouts defined by 3
550 different ILI criteria to determine how our results depended on this somewhat subjective
551 threshold. Based on previous studies of licking dynamics in rats (Davis, 1996) and our own
552 investigation of ILI distributions, we grouped together licks with 200ms or 500ms ILIs into lick
553 'bouts' (also referred to as lick clusters). We also used a more nuanced criterion which we
554 believe better represents active engagement with a lick spout (indicating an ongoing 'stay'
555 decision). This criterion consisted of grouping together adjacent licks in which there was no
556 period >2s between them in which there was no activity on the recording channel. This means
557 that if the rat nose-poked the solution spout in between licks such that the ILI was >2s but there
558 was intervening activity on the channel such that there was no period of >2s of silence, then
559 these licks would be grouped together. We included this criterion since we are primarily
560 concerned in this study with the rats' decisions to leave a solution spout and not on the
561 microstructure of their licking behavior.
562
563 ***Measurement of palatability***
564 To measure the palatability of each concentration of NaCl, we analyzed data exclusively from
565 sessions where a solution was paired with itself. The palatabilities were defined relative to
566 water such that the relative palatability of solution X was:

567 $$Palatability(X) = \frac{N_{licks}(X)}{N_{licks}(dH2O)}$$

568 where $N_{licks}(X)$ is the total number of licks to tastant X across both sessions when X was paired
569 with itself. $N_{licks}(H2O)$ is the same except for H2O only sessions.

570

571 ***Linear and logistic regression models***

572 To assess the impact of the palatability of the currently sampled or alternative solution on the
573 current bout duration, we performed multilinear regressions using MATLAB's *regress* function
574 to predict bout duration with both palatabilities as factors. This was done for all bouts together
575 as well as for subsets of bouts depending on if they were 'early' or 'late' in a session or
576 following a stay or switch decision.

577

578 As one method of measuring the impact of current/alternative palatability on switch
579 probability, we performed logistic regression using MATLAB's *fitglm* function to predict a switch
580 (0 or 1) with the last sampled solution's and alternative solution's palatabilities as factors.

581

582 ***Separating early and late bouts***

583 We separated bouts for each session on a per-animal basis into 'early' or 'late' bouts by
584 analyzing the 2nd derivative of the cumulative distribution of lick times across all sessions. First,
585 a smoothed probability density function of lick onset times was computed using MATLAB's
586 ksdensity function with a bandwidth of 200s (controlling the amount of smoothing). The
587 cumulative density function of this pdf was then computed and its 2nd derivatives
588 approximated. The time point with the minimum 2nd derivative was then used as the divider
589 between early and late bouts.

590

591 ***Statistical tests***

592 Unless otherwise stated, all z and p-values reported in this paper are from the Wilcoxon signed
593 rank test performed using MATLAB's ***signrank*** function. Tests of whether the median of a
594 distribution is significantly positive/negative utilized the right/left-tailed test respectively. Tests
595 of differences between distributions were done using a paired test where data points were
596 paired by animal or, in the case of the spiking model, points were paired by network.
597
598 ***Simulation protocol***
599 Simulations were carried out using a recently published model (Ksander et al., 2021). In brief,
600 leaky integrate-and-fire neurons were designated excitatory or inhibitory and assigned either to
601 a group whose activity promoted a continuous decision of "Stay" at the current stimulus or a
602 group whose activity promoted a decision to "Leave" the stimulus. In the original paper the
603 "Leave" group of cells was denoted "Switch" as we had assumed that leaving one stimulus
604 meant the animal had to switch to the alternative. We produced new simulations for this paper
605 to investigate consequences of a "Return" to the same stimulus following a "Leave" decision
606 that ended a bout.
607
608 Connections between types of neurons were arranged in a manner of self-excitation and cross-
609 inhibition such that activity of one type of neurons (*e.g.,* representing "Stay") could maintain
610 itself while at the same time suppressing activity of the other type of neurons (*e.g.,*
611 representing "Leave"). Activity of the "Stay" neurons while suppressing the "Leave" neurons
612 would represent a "Stay" state in which the animal continues to sample a stimulus. Noise
613 fluctuations would irregularly cause a transition from such a "Stay" state to a "Leave" state. We

614 would ensure the “Leave” state was transient by reactivating “Stay” neurons to represent the
615 animal’s commencement of the next sampling bout. As in our behavioral data, such noise-
616 induced transitions to terminate a bout of sampling resulted in an exponential-like distribution
617 of bout durations.
618
619 We assessed two types of model, in one type, the “entice-to-stay” model, the mean bout
620 durations were determined by stimulus-dependent input to excitatory neurons in the “Stay”
621 pool, such that the more palatable the represented stimulus, the greater the input. In the other
622 type, the “repel-to-leave” model, the mean bout durations were determined by stimulus-
623 dependent input to excitatory neurons in the “Leave” pool, such that the more palatable the
624 represented stimulus, the lower the input. We also test both types of model in this work.
625
626 All synapses in the model include synaptic depression, comprising a fast (300 ms) process
627 representing docking of new vesicles after vesicle release and a slow (7 sec) process
628 representing replenishment of a reserve pool of vesicles. Synaptic depression is key in
629 producing the competitive interaction across time as after a period of strong activity the
630 connections that sustain activity are weakened, impacting the response of the network to a
631 subsequent stimulus, until recovery of the supply of vesicles is complete.
632
633 ***Properties of model neurons***
634 Individual neurons were simulated with an exponential leaky integrate-and-fire model
635 (Fourcaud-Trocmé et al., 2003) following the equation:

$$C_m \frac{dV_m}{dt} = \frac{E_l - V_m + \Delta_{th} \exp\left(\frac{V_m - V_{th}}{\Delta_{th}}\right)}{R_m} + G_{syn}\, S_I \left(E_{rev_I} - V_m\right) + G_{syn}\, S_E \left(E_{rev_E} - V_m\right)$$

$$+ G_{ref}(E_K - V_m) + G_{ext_I}\left(E_{rev_I} - V_m\right) + G_{ext_E}\left(E_{rev_E} - V_m\right)$$

where V_m is the membrane potential, C_m is the total membrane capacitance, E_l is the leak potential, R_m is the total membrane resistance, Δ_{th} is the spiking range, V_{th} is the spiking threshold, S is the synaptic input variable, G_{syn} and E_{rev} are the maximal conductance and reversal potential for synaptic connections, G_{ref} is the dynamic refractory conductance, E_K is the potassium reversal potential, and G_{ext} is the input conductance. The "E" and "I" subscripts denote the variables specific to excitatory and inhibitory channels, respectively (e.g. S_E and E_{rev_E} are the synaptic input and reversal variables for excitatory channels; S_I and E_{rev_I} are the corresponding inhibitory variables). This equation simulates the neuron's membrane potential until $V_m > V_{spike}$, at which point the neuron spikes.

When a neuron spikes, V_m is set to the V_{reset} value. Additionally, the neuron's refractory conductance, synaptic output, s, and synaptic depression (noted as D) are updated according to the equations:

$$G_{ref} \mapsto G_{ref} + \Delta G_{ref}$$

$$s \mapsto s + p_R D_{fast}(1 - s)$$

$$D_{fast} \mapsto D_{fast}(1 - p_R)$$

where ΔG_{ref} is the increase in refractory conductance, and p_R is the vesicle release probability following a spike.

In the timestep immediately following a spike, the neuron's membrane potential continues to follow the exponential leaky integrate-and-fire model equation. In this equation the separate excitatory ($S_{E,i}$) and inhibitory ($S_{I,i}$) synaptic inputs for cell i are obtained from the sum of all presynaptic outputs multiplied by the corresponding connection strengths, W_{ij}, from neurons j (see *Network architecture and connections*):

$$S_i = \sum_j W_{ij} s_j,$$

each of which decay with the appropriate (excitatory or inhibitory) synaptic gating time constant τ_S according to:

$$\frac{ds_i}{dt} = -\frac{s_i}{\tau_S}.$$

Likewise, refractory conductance decays with the time constant τ_{ref} according to:

$$\frac{dG_{ref}}{dt} = -\frac{G_{ref}}{\tau_{ref}}$$

The G_{ext} input conductance serves as both noisy-background and stimulus inputs in the same manner. Inputs were modeled as Poisson spike trains with rates r_{noise} and $r_{stimulus}$, which produce input spikes (from all sources) at timepoints $\{t_{sp}\}$. Please note, the noisy-background includes both excitatory and inhibitory spiking input (included in G_{ext_I} and G_{ext_E} , respectively); the r_{noise} parameter specifies the rate for both excitatory and inhibitory background noise. The input conductance values for a given timepoint, t, are updated as:

$$G_{ext} \mapsto G_{ext} + \Delta G_{ext} \delta(t - t_{sp})$$

where the conductance increases by ΔG_{ext} at the time of each input spike. The input conductance otherwise decays with the time constant τ_{ext} according to:

$$\frac{dG_{ext}}{dt} = -\frac{G_{ext}}{\tau_{ext}}.$$

The cellular parameters with values specific to excitatory neurons (e.g. that differ from inhibitory values) are: $E_{rev_E} = 0\ mV$, $\tau_s = 50\ ms$, and $\tau_{ext} = 3.5\ ms$. The complementary values for inhibitory neurons are: $E_{rev_I} = -70\ mV$, $\tau_s = 10\ ms$, and $\tau_{ext} = 2\ ms$. The remaining parameters applicable to both excitatory and inhibitory neurons are: $G_{syn} = 10\ nS$, $p_R = .1$, $\tau_{fast} = 300\ ms$, $\tau_{slow} = 7\ s$, $p_{slow} = .5$, $E_l = -70\ mV$, $E_K = -80\ mV$, $V_{reset} = -80\ mV$, $R_m = 100\ M\Omega$, $C_m = 100\ pF$, $V_{spike} = 20\ mV$, $\Delta G_{ext} = 1\ nS$, $V_{th} = -50\ mV$, $\Delta_{th} = 2\ mV$, $\tau_{ref} = 25\ ms$, and $\Delta G_{ref} = 12.5\ nS$. The Poisson spike-train parameters r_{noise} and $r_{stimulus}$ are described in the next section. Neurons were simulated with a simulation timestep $dt = .1\ ms$.

Synaptic depression

We modeled synaptic depression using two separate timescales, noted in the previous spike-update equations as D_{slow} and D_{fast}. These two variables reflect, respectively, the fraction of the maximum number of vesicles available in the reserve pool and the release-ready pool. Following a spike, the variables recover to a value of one with different timescales, because vesicles regenerate and are replenished slowly in the reserve pool, but may dock and become release-ready much more quickly once available in the reserve pool

Specifically, D_{slow} represents the ratio of currently available reserve-pool vesicles out of the maximum possible, that is $D_{slow} = \frac{N_{pool}}{N_{max}}$. These dock quickly at empty docking sites on the timescale τ_{fast}, but are replaced slowly on the timescale τ_{slow}. D_{fast} represents the ratio of docked vesicles out of total docking sites, that is $D_{fast} = \frac{N_{docked}}{N_{sites}}$. We also incorporate the constant parameter, $f_D = 0.05$, which is equal to the ratio of the number of docking sites to the maximum size of the reserve pool of vesicles, $f_D = \frac{N_{sites}}{N_{max}}$. Only docked vesicles can be released immediately following a spike, such that upon each spike we update $D_{fast} \mapsto D_{fast}(1 - p_R)$ where p_R is the vesicle release probability.

During sustained spiking, the fast-docking can maintain a firing-rate dependent supply of docked vesicles until the reserve pool depletes. Vesicles dock at empty sites according to:

$$\frac{dD_{fast}}{dt} = \frac{\left(D_{slow} - D_{fast}\right)}{\tau_{fast}}$$

Reserve-pool vesicles fill the empty docking sites on the fast timescale τ_{fast}. On the other hand, the reserve-pool regenerates much more slowly according to:

$$\frac{dD_{slow}}{dt} = \frac{(1 - D_{slow})}{\tau_{slow}} - f_D \frac{\left(D_{slow} - D_{fast}\right)}{\tau_{fast}}$$

The first term represents the reserve-pool vesicle regeneration on timescale τ_{slow}. The second term $-f_D \frac{(D_{slow} - D_{fast})}{\tau_{fast}}$ accounts for the vesicles lost due to docking.

Our model reflects the empirical evidence showing the effects of synaptic-depression at short timescales on the order of milliseconds, and longer timescales on the order of seconds (Abbott

717 et al., 1997; Varela et al., 1997); depression timescales on the order of minutes have even
718 reported in non-mammalian animals (Tabak et al., 2000). Additional, recent evidence (Kusick et
719 al., 2020) directly supports our fast-depression mechanism where available vesicles quickly refill
720 empty docking sites. Our model provides a coherent mechanism for both fast-acting and long-
721 lasting synaptic depression effects.
722
723 ***Network architecture and connections***
724 Each network consists of 250 individual neurons, split into two populations of 100 excitatory
725 cells (*i. e.,* "stay" and "switch" populations, E_{stay} and E_{switch}) and two populations of 25 inhibitory
726 cells (I_{stay} and I_{switch}). For each pair of connected populations (or for self-connected excitatory
727 populations) pairs of cells were connected probabilistically with a probability,
728 $P(connection) = .5$. The strength of connections was symmetric across "stay" and "switch"
729 populations but depended on whether presynaptic or postsynaptic cells were excitatory or
730 inhibitory, as indicated in Table 1.
731
732 **Code Availability**
733 The code used to simulate our model is freely available online at
734 https://github.com/johnksander/naturalistic-decision-making
735
736 **Table 1. Model neuron parameters.**

Name	Description	value

$\boldsymbol{E_{rev}}$	Reversal potential	Excitatory cells: $0\ mV$ Inhibitory cells: $-70\ mV$
$\boldsymbol{E_l}$	Leak potential	$-70\ mV$
$\boldsymbol{E_K}$	Potassium potential	$-80\ mV$
$\boldsymbol{R_m}$	Membrane resistance	$100\ M\Omega$
$\boldsymbol{C_m}$	Membrane capacity	$100\ pF$
$\boldsymbol{\tau_s}$	Synaptic gating timescale	Excitatory cells: $50\ ms$ Inhibitory cells: $10\ ms$
$\boldsymbol{V_{reset}}$	Reset membrane potential	$-80\ mV$
$\boldsymbol{V_{spike}}$	Spike threshold	$20\ mV$
$\boldsymbol{\tau_{ext}}$	noisy-background conductance timescale	Excitatory cells: 3.5 ms Inhibitory cells: 2 ms
$\boldsymbol{G_{syn}}$	Synaptic max conductance	$10\ nS$
$\boldsymbol{\tau_{fast}}$	Fast depression timescale	$300\ ms$
$\boldsymbol{\tau_{slow}}$	Slow depression timescale	$7\ s$
$\boldsymbol{p_R}$	Vesicle release probability	.1
$\boldsymbol{f_D}$	Ratio of max docked vesicles to max reserve vesicles	.05
$\boldsymbol{D_{fast}}$	Ratio of docked vesicles out of max possible	$\frac{N_{docked}}{N_{sites}}$
$\boldsymbol{D_{slow}}$	Ratio of reserve- vesicles out of max possible	$\frac{N_{pool}}{N_{max}}$
$\boldsymbol{\Delta G_{ext}}$	Conductance step-increase to external input spike	$1\ nS$
$\boldsymbol{V_{th}}$	exponential spiking-term threshold	$-50\ mV$

$\boldsymbol{\Delta_{th}}$	spiking range	$2\ mV$
$\boldsymbol{\tau_{ref}}$	Refractory conductance timescale	$25\ ms$
$\boldsymbol{\Delta G_{ref}}$	Step change in refractory conductance	$12.5\ nS$
$\boldsymbol{dt}$	Simulation timestep	$.1\ ms$

A Model summary	
Populations	Stay: 1 excitatory, 1 inhibitory Leave: 1 excitatory, 1 inhibitory
Connectivity	Within-pool (stay or leave): I-to-E and recurrent E-to-E Cross-pool (stay-to-leave or leave-to-stay): E-to-I
Neuron model	Exponential Leaky Integrate and Fire (ELIF) with dynamic refractory conductance
Synapse model	Conductance based, step increase followed by exponential decay
Plasticity	Depression with two timescales
Input	Noisy background input: fixed-rate Poisson spike trains to all cells Stimuli: Poisson spike trains to E-stay and E-leave cells
Measurements	Spike trains, activity state-durations, connection strengths

B Populations		
Name	**Elements**	**Size**
E-stay	ELIF neurons	100
I-stay	ELIF neurons	25

E-leave	ELIF neurons	100
I-leave	ELIF neurons	25
Noisy background input	Poisson trains	500
Aversive stimulus	Poisson trains	100
Hedonic stimulus	Poisson trains	100

739

C Connectivity			
Name	**Source**	**Target**	**Pattern**
E-to-I	E-stay E-leave	I-leave I-stay	Random, $p = .5$, model-dependent fixed weight: 'Entice' network 0.0909 'Repel' network 0.4242
I-to-E	I-stay I-leave	E-stay E-leave	Random, $p = .5$, model-dependent weight: 'Entice' network 9.6192 'Repel' network 9.4939
E-to-E	E-stay, E-leave	E-stay, E-leave	Random, $p = .5$, fixed weight, $W^{EE} = 0.0405$

740

D Neuron and Synapse Model	
Name	LIF neuron
Type	Dynamic leaky integrate-and-fire with dynamic refractory conductance

Subthreshold dynamics	$C_m \frac{dV_m}{dt} = \frac{E_L - V_m + \Delta_{th}\exp\left(\frac{V_m - V_{th}}{\Delta_{th}}\right)}{R_m} + G_{syn} \cdot S_I \left(E_{rev_I} - V_m\right)$ $+ G_{syn} \cdot S_E \left(E_{rev_E} - V_m\right) + G_{ref}(E_K - V_m) + G_{ext_I}\left(E_{rev_I} - V_m\right)$ $+ G_{ext_E}\left(E_{rev_E} - V_m\right)$ $\frac{dG_{ref}}{dt} = -\frac{G_{ref}}{\tau_{ref}}$ $\frac{dG_{ext}}{dt} = -\frac{G_{ext}}{\tau_{ext}}$
Spiking	If $V_m > V_{spike}$: 1. Emit spike with timestamp t 2. $G_{ref} \mapsto G_{ref} + \Delta G_{ref}$ 3. $V_m \mapsto V_{reset}$
Synapse	$S_i = \sum_j W_{ij} s_j$ following a spike by neuron i: $s_i \mapsto s_i + p_R D_{fast}(1 - s_i)$

	$D_{fast,i} \mapsto D_{fast,i}(1 - p_R)$ Between spikes: $\frac{ds_i}{dt} = -\frac{s_i}{\tau_S}$ $\frac{dD_{fast,i}}{dt} = \frac{\left(D_{slow,i} - D_{fast,i}\right)}{\tau_{fast}}$ $\frac{dD_{slow,i}}{dt} = \frac{\left(1 - D_{slow,i}\right)}{\tau_{slow}} - f_D \frac{\left(D_{slow,i} - D_{fast,i}\right)}{\tau_{fast}}$

741

F Input	
Type	**Description**
All external spiking input	Input spikes increase conductance: $G_{ext} \mapsto G_{ext} + B \cdot \Delta G_{ext}$ Conductance G_{ext} decays: $\frac{dG_{ext}}{dt} = -\frac{G_{ext}}{\tau_{ext}}$
Background noisy input	One excitatory spike-train per neuron, and one inhibitory spike-train per neuron (all 1540 Hz Poisson spike-trains).
Stimulus	One excitatory spike-train per neuron in the E-Stay pool (“Entice” network) or the E-Leave pool (“Repel” network). In any simulated

	preference test two distinct stimulus strengths were used from the following sets of three: “Entice” network stimulus strengths of increasing palatability were 94.35Hz, 377.4Hz, 660.45Hz. “Repel” network stimulus strengths of increasing palatability were 198.62Hz, 113.5Hz, 28.35Hz.

742

743

G Measurements
Active state: when mean difference between E-stay and E-leave excitatory synaptic gating exceeds .02 for 50ms (consecutively).
State duration/sampling duration: time between state transitions (i.e. transitioning from E-stay to E-leave active state).

744

745 ***Network states and stimuli***

746 A network’s active state was evaluated by comparing the mean values of synaptic output, s_E,
747 averaged across all excitatory cells in each of the two excitatory populations. Specifically, when
748 the difference between the mean output of the previously less active excitatory population
749 exceeded that of the previously more active excitatory population by a threshold of 0.02
750 consistently for 50ms, we recorded a state change.

751

752 We did not simulate the animal’s behavior in between bouts of sampling a stimulus. Once the
753 excitatory neurons in the “switch” population (E-switch cells) were recorded as more active

than those in the “stay” population, using the threshold mentioned above, we removed the stimulus input to the network. 100 ms later, we induced a subsequent transition back to the “stay” state to represent the animal initiating a new bout of stimulus sampling. The transition back to sampling was accomplished by halving the noisy background input to E-switch cells until the network transitioned again to the “stay” state. At all other times in simulations, the noisy background input remained constant. Once a transition to the “stay” state was recorded (by excitatory cells in the “stay” population being more active than those in the “switch” population) input stimulus was applied to indicate the next bout of sampling. The choice of subsequent next stimulus was probabilistic, with 50% probability of each of the pair being compared in the simulated preference test. Individual taste preference task simulations lasted 1500 seconds total. Each simulation compared sampling bout durations in response to two stimuli each with a fixed value across the session. For a given network the stimulus inputs targeted the same population for all sessions.

To produce linear regression coefficients in Figure 10, we regressed the log of the state duration as a function of the stimulus strengths used, because state durations depend exponentially on stimulus strengths in our model, which is based on noise-induced transitions between attractor states (Kramers, 1940; Miller & Wang, 2006).

References

Abbott, L. F., Varela, J., Sen, K., & Nelson, S. (1997). Synaptic depression and cortical gain control. *Science*, *275*(5297), 221-224.

Barack, D. L., Chang, S. W. C., & Platt, M. L. (2017). Posterior Cingulate Neurons Dynamically Signal Decisions to Disengage during Foraging. *Neuron*, *96*(2), 339-347 e335. https://doi.org/10.1016/j.neuron.2017.09.048

Bateson, M., & Kacelnik, A. (1996). Rate currencies and the foraging starling: the fallacy of the averages revisited. *Behavioral Ecology*, *7*(3), 341-352. https://doi.org/10.1093/beheco/7.3.341

Blanchard, T. C., & Hayden, B. Y. (2014). Neurons in dorsal anterior cingulate cortex signal postdecisional variables in a foraging task. *J Neurosci*, *34*(2), 646-655. https://doi.org/10.1523/JNEUROSCI.3151-13.2014

Blanchard, T. C., Pearson, J. M., & Hayden, B. Y. (2013). Postreward delays and systematic biases in measures of animal temporal discounting. *Proc Natl Acad Sci U S A*, *110*(38), 15491-15496. https://doi.org/10.1073/pnas.1310446110

Charnov, E. L. (1976). Optimal foraging, the marginal value theorem. *Theor Popul Biol*, *9*(2), 129-136. https://doi.org/10.1016/0040-5809(76)90040-x

Constantino, S. M., & Daw, N. D. (2015). Learning the opportunity cost of time in a patch-foraging task. *Cogn Affect Behav Neurosci*, *15*(4), 837-853. https://doi.org/10.3758/s13415-015-0350-y

Davis, J. D. (1996). Deterministic and probabilistic control of the behavior of rats ingesting liquid diets. *Am J Physiol*, *270*(4 Pt 2), R793-800. https://doi.org/10.1152/ajpregu.1996.270.4.R793

Davis, J. D., & Smith, G. P. (1992). Analysis of the microstructure of the rhythmic tongue movements of rats ingesting maltose and sucrose solutions. *Behav Neurosci*, *106*(1), 217-228.

Fourcaud-Trocmé, N., Hansel, D., van Vreeswijk, C., & Brunel, N. (2003). How spike generation mechanisms determine the neuronal response to fluctuating inputs. *J Neurosci*, *23*(37), 11628-11640. https://doi.org/10.1523/jneurosci.23-37-11628.2003

Hayar, A., Bryant, J. L., Boughter, J. D., & Heck, D. H. (2006). A low-cost solution to measure mouse licking in an electrophysiological setup with a standard analog-to-digital converter. *J Neurosci Methods*, *153*(2), 203-207. https://doi.org/10.1016/j.jneumeth.2005.10.023

Hayden, B. Y., Pearson, J. M., & Platt, M. L. (2011). Neuronal basis of sequential foraging decisions in a patchy environment. *Nat Neurosci*, *14*(7), 933-939. https://doi.org/10.1038/nn.2856

Kramers, H. A. (1940). Brownian motion in a field of force and the diffusion model of chemical reactions. *Physica*, *7*(4), 284-304. https://doi.org/https://doi.org/10.1016/S0031-8914(40)90098-2

Ksander, J., Katz, D. B., & Miller, P. (2021). A model of naturalistic decision making in preference tests. *PLoS Comput Biol*, *17*(9), e1009012. https://doi.org/10.1371/journal.pcbi.1009012

Kusick, G. F., Chin, M., Raychaudhuri, S., Lippmann, K., Adula, K. P., Hujber, E. J., Vu, T., Davis, M. W., Jorgensen, E. M., & Watanabe, S. (2020). Synaptic vesicles transiently dock to refill release sites. *Nat Neurosci*, *23*(11), 1329-1338. https://doi.org/10.1038/s41593-020-00716-1

Miller, P., & Wang, X.-J. (2006). Stability of discrete memory states to stochastic fluctuations in neuronal systems. *Chaos (Woodbury, N.Y.)*, *16*(2), 026109-026109. https://doi.org/10.1063/1.2208923

Pearson, J. M., Hayden, B. Y., & Platt, M. L. (2010). Explicit information reduces discounting behavior in monkeys. *Front Psychol*, *1*, 237. https://doi.org/10.3389/fpsyg.2010.00237

Pearson, J. M., Watson, K. K., & Platt, M. L. (2014). Decision making: the neuroethological turn. *Neuron*, *82*(5), 950-965. https://doi.org/10.1016/j.neuron.2014.04.037

Sadacca, B. F., Rothwax, J. T., & Katz, D. B. (2012). Sodium concentration coding gives way to evaluative coding in cortex and amygdala. *J Neurosci*, *32*(29), 9999-10011. https://doi.org/10.1523/JNEUROSCI.6059-11.2012

Stephens, D. W. (2002). Discrimination, discounting and impulsivity: a role for an informational constraint. *Philos Trans R Soc Lond B Biol Sci*, *357*(1427), 1527-1537. https://doi.org/10.1098/rstb.2002.1062

Stephens, D. W., & Anderson, D. (2001). The adaptive value of preference for immediacy: when shortsighted rules have farsighted consequences. *Behavioral Ecology*, *12*(3), 330-339. https://doi.org/10.1093/beheco/12.3.330

Tabak, J., Senn, W., O'Donovan, M. J., & Rinzel, J. (2000). Modeling of spontaneous activity in developing spinal cord using activity-dependent depression in an excitatory network. *J Neurosci*, *20*(8), 3041-3056. https://www.ncbi.nlm.nih.gov/pubmed/10751456

Varela, J. A., Sen, K., Gibson, J., Fost, J., Abbott, L., & Nelson, S. B. (1997). A quantitative description of short-term plasticity at excitatory synapses in layer 2/3 of rat primary visual cortex. *Journal of Neuroscience*, *17*(20), 7926-7940.