Title

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# Abstract

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# Statement of Contribution

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| Signed: |  |
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Date: /2017

# **CHAPTER 1: INTRODUCTION**

30% of the word count is for background/literature review

## Overview (is a title needed?)

Opening statement - start with concept of consciousness – hard problem of consciousness, mention that there are existing theories of consciousness, one which somewhat tackles the hard problem is IIT. The aim of this project is threefold: to test if IIT’s proposed measure is larger during consciousness (or conversely reduced under anaesthesia), to compare it’s latest, computationally expensive derivation to a more practical version, and to compare the derivation of phi to a past finding in the same data. This project aims to investigate the validity of IIT’s measure of consciousness by applying it to local field potentials recorded from the fly brain.

## Theories of Consciousness

## Integrated Information Theory

Information is what we ‘get out’ of an event which occurs. If the probability of some event occurring is 1 (i.e. it always occurs), then the occurrence of that event gives no information (as we already know that it always occurs). In this case, the information we get from the event occurring is 0. This is the lower bound of information (however, some advocate for the utility of negative information)

Entropy is a measure of uncertainty. For example, a coin flip has two possible outcomes. With two possible outcomes, uncertainty (i.e. entropy) would be maximised if the coin was unbiased – we wouldn’t be able to predict the outcome any better than chance. If the coin was biased however, say towards heads, then the outcome is less uncertain as it is more likely to be heads. In the extreme case where the outcome is always heads, there would be no uncertainty at all – in this case there is only really one outcome. If we know that the coin is biased in such a manner, observing the outcome would give us no information (as we practically already know the outcome). If we knew that the coin was slightly biased, we would get a little information. Conversely, if the coin was fair, then observing the outcome would give us information, i.e. the outcome. It is intuitive that the more ‘uncertain’ a set of events is, the more information we get from any of the events occurring.

Conditional entropy of some variable is the entropy of that variable given a fixed value of another variable.

IIT posits that integrated information phi is consciousness. To understand what is meant by “integrated information”, perhaps it is a good idea to break it into two parts: information and integration. Information may be understood as a reduction in uncertainty. As an example, let’s consider a system of two simple neurons. At any one timepoint, each of the two simple neurons is either firing or not firing. Thus at any timepoint, the system takes one of four states, as illustrated in Figure. If we know or consider nothing more about the two neurons, at any timepoint t we could only guess their state at chance accuracy (i.e. in this scenario we would have a one in four chance of guessing correctly), even if we knew their past state (at t-1) or even future state (at t+1). This uncertainty is referred to as entropy. However, if we knew that second of the neurons at time t always assumed the state of the first neuron at time t-1, considering the past system state would essentially allow us to eliminate two possibilities for time t, increasing the chances of a correct guess (which would now be one in two). This new uncertainty, given a fixed condition (knowing the first neuron at t-1) is referred to as the conditional entropy (the entropy conditioned upon a fixed event). The reduction of uncertainty by considering the past state (consequently increasing our guess chance from ¼ to ½) is referred to as mutual information. In our specific case, because our information is derived from entropies before and after taking into account the past state, it is formally referred to as mutual information (or information gain – mutual information and information gain are equivalent).

The modifier “integrated” specifies that any information gain (from considering the system state at some other time) should be due to dependencies among elements within the system. A simple example to demonstrate this: consider two brains as a single system. While considering the past of both brains allows us to better predict the present states within both brains, we can also consider the two brains independently and predict just as better. In other words, considering the two brains together gives us no additional information than just considering one at a time, and so there is no integration and thus no integrated information.

The last iteration of IIT (3.0) updated both of how to calculate information and how to assess integration. Information is now assessed using the earth mover’s distance instead of Kullback-Leibler divervence (with KL-divergence being the generally accepted distance measure, but not metric, in information theory), and integration is now considered in a bidirectional manner.

## Integrated Information from the Decoding Perspective (include as subheading under IIT?)

### Mutual Information

### Condition Mutual Information

## Loss of Consciousness and Feedback Disruption Under Anaesthesia

## LFP

## Aims and Hypotheses (in a separate section?)

G1: air vs iso

Compare air to iso at each parameter: channels-used and tau-lag

Description for phis via LME: assess main effect of condition, channels used, and lag, accounting for the nested design

If using ANOVA, (i.e. not distinguishing between sets), maybe not necessary to conduct t-tests per set?

Figures: average phi at all parameters, for all sets

G2: 3 vs star

Correlation between phi3 and phistar at each channels-used and tau-lag

G3

# **CHAPTER 2: EXPERIMENTAL METHODS AND RESULTS**

## Method

### Experimental Procedure

The data used in this project is a subset of the data collected and preprocessed previously in {Cohen 2016}, where the full experiment is described. Here I only detail methods relevant to the dataset used in the present project.

Animal preparation. Thirteen female laboratory-reared Drosophila melanogaster flies (Canton S wild type, 3-7 days post eclosion) were collected under cold anaesthesia and tethered to a tungsten rod. Flies were glued dorsally to the rod using dental cement (Synergy D6 FLOW A3.5/B3, Coltène Whaledent) which was cured with blue light. The flies’ wings were also glued to the rod in order to prevent wingbeats during recording, and dental cement was applied to the neck to stabilise the head. Tethered flies were positioned above a 45.5 mg air-supported Styrofoam ball, setup similarly to {Paulk 2013}, and thus were able to walk in place.

Electrode probe insertion. Linear silicon probes with 16 electrodes (Neuronexus Technologies) were inserted laterally into the fly’s eye, perpendicular to its curvature, with the electrode recording sites facing posteriorly. Insertion was performed with the aid of a micromanipulator (Märzhäuser). Probes had an electrode site separation of 25 µm (3mm-35-177) and measured 375 µm from base to tip. As a reference electrode, a sharped fine tungsten wire (0.01 inch diameter, A-M Systems) was placed in the thorax. Recordings were made using a Tucker-Davis Technologies multichannel data acquisition system with a 25 kHz sampling rate. To ensure consistent probe insertion depth, probes were inserted until all electrodes were recording neural activity. This was confirmed by presenting a flickering visual stimulus (with spectral peak at 460 nm and 30nm half-peak width; flickering at 1 and 13 Hz), and subsequently observing steady state visually evoked potentials (SSVEPs) at the most peripheral electrode. The probe was then retracted until the most peripheral electrode showed little to no neural activity. Probe insertion in this manner does not seem to affect fly locomotion {Paulk 2013}.

Isoflurane delivery. Isoflurane was delivered from an evaporator (Mediquip) onto the fly through a connected rubber hose. The isoflurane was delivered at a constant flow of 2 l/min and continuously vacuumed from the opposite side of the fly. Actual concentration near the fly body was either 0 vol% (air condition) or 0.6 vol% (isoflurane condition) as estimated following the gas chromatography procedure described by {Kottler 2013} for measuring isoflurane concentration.

Experimental protocol. The complete experimental procedure is described in {Cohen 2016}. Here I briefly describe the procedure relevant to the data used in this project. An experiment consisted of two blocks: one for the air condition, followed by one for the isoflurane condition. Each block started with a series of air puffs, followed by 18 s of rest, 248 s of visual stimuli, another 18 s of rest, and finally a second series of air puffs. Isoflurane was administered immediately after completion of the first block (i.e. after the last air puff), and flies were left for 180 s to adjust to the new concentration before beginning the second block. The data used in this project corresponds to the 18 s period between the end of the first series of air puffs and the beginning of the visual stimuli.

Local field potential preprocessing. LFPs were recorded at 25 kHz and downsampled to 1000 Hz. Electrodes were bipolar rereferenced by subtracting neighbouring electrodes, resulting in 15 signals. Hereafter these signals will be referred to as “channels”. The 18 s of data for each condition was split into 2.25s segments, giving 8 “trials” of 2250 samples each. Finally, line noise at 50 Hz was removed using the *rmlinesmovingwinc.m* function of the Chronux toolbox {<http://chronux.org/>; Mitra and Bokil, 2007} with three tapers, a windows size of 0.7 s, and a step size of 0.35 s.

### Φ3 Computation

Discretisation. IIT 3.0 has not yet been extended to be applicable to continuous variables. As the calculation of Φ in IIT 3.0 requires discrete variables, rereferenced LFPs were binarised using a global median split. For each fly and condition, median sample across trials was identified for each channel. Samples were then replaced with a 1 if greater than the median, and 0 otherwise.

Channel selection. Given that the time to calculate phi grows exponentially with the number of elements in a candidate system, I calculated phi only for systems consisting of up to four channels (i.e. systems of 2, 3, or 4 channels). For these systems, phi was calculated across all channel combinations (i.e. 15 choose 2, 15 choose 3, and 15 choose 4).

TPM Construction. IIT characterises the difference between the

Φ calculation. Phis was calculated using the PyPhi package for Python 3.6. The details of computing phi are provided in {Oizumi 2014}, so I here will give a brief summary of the calculation process.

### Φ\* Computation

Phistar was calculated in MATLAB 2017a, using a toolbox which implemented phistar calculation in a previous project {<https://github.com/amhaun01/phipattern>, Haun}. The details of computing phistar are given in {Oizumi 2016}, so once again I will provide only a summary of the process.

Phistar can be summarised relatively simply. It is the difference between the mutual information of a whole system, when considering all connections between its parts, and the mutual information of a partitioned system, where we ignore some set of connections in the original system.

## Results

While it is unclear whether flies are “conscious” in that they have phenomenological experience, isoflurane reduces behavioural stimuli to noxious stimuli (perhaps this should be covered in the introduction, and if so, doesn’t need to be mentioned here? Or maybe just a reminder that responsiveness diminished under isoflurane?) Analyses were conducted using MATLAB 2017a and MATLAB 2015b (simulated likelihood ratio tests, via MASSIVE).

### Phi-3 greater during wakefulness

t-tests conducted for each channel combination (with FDR corrected threshold of q=0.1) revealed greater phi during the air condition for many channels, as is displayed in Figure x. Meanwhile, x% had lower phi in the air condition. To confirm an overall effect, a linear mixed effects model was employed. A linear mixed effects model was used to account for the channel combinations being crossed across flies. Thus, random intercepts for fly and the interaction between fly and channel combination was included in the model. Fixed effects of condition, lag, and channels used were also included. To address linearity and normality (information theoretic measures were heavily skewed), log transformed values were used for statistical testing. To test for fixed effects, likelihood ratio tests comparing the full model with a null model lacking the fixed effect were used. As suggested by Figure 1, condition indeed had a significant effect on the magnitude of phi, as did lag and number of channels used.

### Equal likelihood of MIP cuts

Here we defined feedback as an influence from the centre channels to the peripheral channels. As it is not immediately obvious as to whether a partitioning of three channels or more is feedback or not, we limited this analysis to combinations consisting of only two channels. This parallels the two channel nature of the GC analysis which was conducted previously by {Cohen 2016}.

### Moderate correlation with phi\*

As with phi-3, an linear mixed effects model was used to assess the fixed effects of condition, lag, and channels used. Figure x shows the values at each channel combination (no t-tests survived correction for multiple comparisons at q=0.1). This was repeated for mutual information and entropy.

To confirm this, phi-3 was regressed onto phi-star (via lme). Correlations were calculated at each channel combination.