Toward a Portable, Self-Administered Critical Flicker Frequency Test

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Abstract

The UbiComp community's research in mental health has often focused on depression, but we believe there are many additional opportunities. As participants in this workshop, we will present our initial work to create a portable and self-administered version of the Critical Flicker Frequency (CFF) test. We focus on hepatic encephalopathy, but the test has potential for long-term self-monitoring in a variety of conditions impacting mental health, including cerebro-organic syndromes, multiple sclerosis, Alzheimer's disease, chronic fatigue, and testing of psychoactive drugs. CFF can detect transient effects on the brain and retina which serve as indicators for the above conditions. However, commercial devices for performing the CFF test are expensive and unwieldy. This limits clinical availability of CFF testing, prevents frequent self-administered testing, and reduces access. We explore the possibility of an affordable and portable device for self-administered CFF testing, implemented using commodity components paired with a mobile phone app. Such a device surfaces many future research challenges analogous to those in other areas of mental health. As background for discussions in this workshop, we discuss our initial exploratory design efforts and potential future steps for the project.

Author Keywords

Critical Flicker Frequency, Hepatic Encephalopathy, Mental Health, Self-Monitoring, Prototyping.
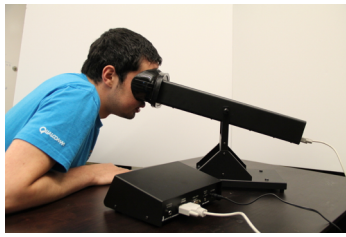
Figure 1: The Lafayette Flicker Fusion System. Viewing box on the top left, controller on the top right.

Viewing chamber dimensions: 330 x 130 x 70 mm

Critical Flicker Frequency

Critical Flicker Frequency (CFF) testing can be used in detecting a variety of neuro-psychological abnormalities, from visual signal processing (e.g., retinal gliopathy) to cognitive functions. CFF testing has therefore been applied to the study of several neurological disorders (e.g., multiple sclerosis, Alzheimer's disease). It is particularly apt for the study of alterations in visual signal processing, and is also suitable for the detection of arousal or attention abnormalities [12].

CFF is defined as the frequency at which an intermittent light stimulus (i.e., a blinking light) appears completely fused to the observer (i.e. steadily on, not flickering). The CFF phenomena depends on both the brain and the retina, so transient effects in either can affect a person's critical flicker fusion frequency threshold. The CFF test has been in limited clinical and research use for over a decade, and its diagnostic accuracy has been evaluated in a number of reviews [2,9,10,15]. Early research applying the CFF test established a set of standard testing conditions that have been adopted by subsequent work [7,15]. These conditions are also implemented in commercially available devices, such as the Hepatonorm Analyzer[1], the Lafayette Flicker Fusion System[2] (Figure 1), and the Schuhfried Flicker Fusion Analyzer[3].

Standardized application of the CFF test is done in a quiet, semi-darkened room. A white light source is used to generate square waves with 50% duty cycle. Step rate for increasing or decreasing frequency is 0.1, 0.5, or 1 Hz/sec between 25 Hz and 60 Hz. Stepwise increase

from 25 Hz is used to determine the fusion frequency threshold (i.e., when the light is perceived to stop flickering), while stepwise decrease from 60Hz is used to determine the flicker frequency threshold (i.e., when the light is perceived to start flickering). The test is usually repeated 6 to 8 times to calculate the mean threshold value and also estimate the standard deviation of the measurement. The whole procedure can therefore take about 10 minutes to complete [7].

MINIMAL HEPATIC ENCEPHALOPATHY

A person's ability to perceive flicker fusion frequencies corresponds to the efficiency of both the visual cortex and the cerebral cortex. One application of CFF is detection of minimal hepatic encephalopathy (MHE). MHE occurs in people with chronic liver diseases (e.g., cirrhosis, hepatitis). People with MHE perform abnormally primarily due to altered neuronal communication resulting in delayed information processing. This is a result of astrocyte (i.e., brain cell) swelling due to the liver's inability to clear toxins from the body (e.g., ammonia) [7]. CFF testing offers the potential to detect this impact on visual/mental function.

As an early form of overt Hepatic Encephalopathy, MHE is especially challenging because subtle deficits in cognitive functions and psychomotor abnormalities can only be detected by specialized psychometric tests [3]. Despite the subtlety of the symptoms, MHE has been associated with negative impact on quality of life [13] as well as driving impairment and increased chance of road traffic accidents [6,16]. In later stages, MHE can also lead to overt Hepatic Encephalopathy, resulting in increased mortality [5]. Improved support for detecting and self-monitoring MHE could enable earlier treatment, reducing its impact and preventing escalation.

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[1] http://www.nevolab.de/portfolio/hepatonorm-analyser/

[2] http://www.lafayettelifesciences.com/product_detail.asp?itemid=36

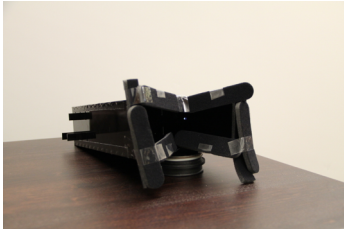[3] http://www.schuhfried.com/test/FLIM

Figure 2: Viewing box prototype, inspired by approaches like Google Cardboard and modeled after the form of the Lafayette system. Slits on the side of the box to allow for variable distance between the light source and the person. The box can be rested on a surface while taking a test.

Dimensions: 330 x 150 x 70 mm

Among several diagnostic tests for MHE, there is no universally accepted standard [15]. The de-facto standard suggested by the Expert Working Group in 1998 is the psychometric hepatic encephalopathy score (PHES), a neuropsychological test [10]. It is a selection of five validated psychometric test batteries [1,11,14]. Although widely used, this test has several limitations: it is time consuming, prone to bias from disturbances, due to mood, interaction with the tester, and language. It is also impacted by learning effects [15], and is therefore inappropriate for long-term self-monitoring.

Flicker perception at frequencies lower than 38-39Hz correlates with the presence of MHE, and so a CFF test protocol has been developed to help screen for MHE. The test is usually conducted by applying descending and ascending protocols, with flicker frequency gradually decreased or increased in the range between 25 and 60Hz. This procedure, called a method of limits, is usually repeated 6 to 8 times and the result is calculated based on the mean outcome [11].

The CFF test has only a moderate pooled sensitivity (i.e., the ability to correctly identify those with the disease) of 61% (95% CI: 55–67), but a good specificity (i.e., the ability to correctly identify those without the disease) of 79% (95% CI: 75–83) [7]. Due to these properties, the test is considered good for discriminating patients with MHE from those without MHE, and is most appropriate as a screening tool [15]. Such screening use has been proposed prior to the current psychometric tools, or to be used alongside these tools, but not necessarily as a replacement due to the risk of false negative results [15].

Opportunities for a Portable CFF Test

The aim of our prototyping is to considerably reduce device cost, improve the controller to make testing more self-administrable, and improve the physical form to reduce burdens of self-monitoring. Successful prototyping of new portable approaches to self-administering a CFF test will then enable future research in long-term patient self-monitoring and potential improvements in testing (e.g., using personal baselines or measurement over time to improve on current sensitivity and specificity).

Design & Implementation

In our efforts to explore testing using a mobile phone, we first sought to develop a software-only CFF test. Finding barriers to such an implementation, we developed hardware prototypes using commodity components to explore smaller and more portable form factors.

BARRIERS TO A SOFTWARE-ONLY TEST

Motivated by recent success using the existing sensors of a phone to obtain physical measures (e.g., step count[4], heart rate[5]) and to perform medical diagnostic tests (e.g., jaundice [4], lung function [8]), we first sought to develop a CFF test using only the hardware present in a typical phone. For example, one could imagine using the LED provided for the camera's flash to perform the test. However, we found current phones do not provide control of the LED at the necessary frequencies (i.e., 25 to 60Hz). We also considered the display as a possible alternative, but a similar issue arises where the refresh rate of the screen does not allow generating the necessary frequencies. These could eventually be addressed with additional phone capabilities, motivated

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[4] http://www.fitbit.com

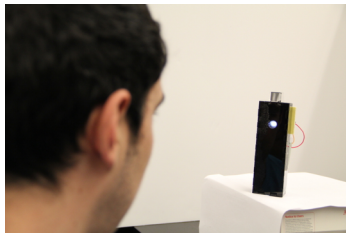[5] http://www.azumio.com/s/instantheartrate/index.html

Figure 3: Handheld prototype, used to examine whether a viewing box is necessary. The device is intended to be placed on a flat surface aligned with the eye.

Dimensions: 140 x 40 x 40 mm

in part by efforts like our research, but we shifted our current focus to pairing with a hardware device.

PROTOTYPING PHYSICAL FORM AND A SELF-ADMINISTERED TEST
Given limitations of the phone itself as a possible solution, we decided to focus on wirelessly pairing a phone with a testing device. We used the Lafayette Flicker Fusion System[2] (Figure 1) as a benchmark for comparison, and have iteratively developed two prototype devices.

We first built a viewing box similar to that used in the Lafayette system (Figure 2). Our viewing box is designed to allow a variable distance between the light source and a person by placing the light source at different locations in the box. Given the dimensions of the box and its relatively simple design, we opted to laser cut the box from an opaque black sheet of acrylic (e.g., rather than 3D printing it). We use a cool white LED[6] capable of a wide range of luminous intensity (i.e., 28 to 64cd), with a 1500 grit diffuser[7] in front of the LED. For the control module, we use a RFduino[8] due to its compact size and built-in support for Bluetooth Low Energy. Another benefit is RFduino's two-way communication API, which makes it easier to prototype a mobile app (e.g., using associated sample apps). We can use such apps to test different potential protocols for self-administering the test.

A test is initiated by powering on the device and launching the phone app, which finds and connects to the device. After it is connected, the prototype app currently allows selection of a protocol for administering the test. A person places their face against the viewing box and taps

anywhere on the phone screen to start the test. For the method of limits protocol, the LED frequency starts at 25 Hz and increases by 1 Hz/s. A voice prompt asks the person to tap anywhere on the phone's screen when they perceive the LED is fused (i.e., stops flickering). After the person taps, the frequency starts at 60 Hz and decreases by 1 Hz/s. A voice prompt asks the person to tap anywhere on the phone screen when they perceive the LED flickering. When the person taps, a voice prompt asks them to remove the viewing box and check results on the phone. This process would repeat 6 to 8 times, with the result being the mean across measurements.

Our initial informal and exploratory testing found similar results using our prototype and the Lafayette device. We also began exploring how to make the viewing box more compact, which could make it more portable and less cumbersome. As part of this, we conducted a literature review that found no fixed requirements for the viewing box. We hypothesized that the box helps keep the light source and a person's eye aligned while reducing background visual noise and controlling for ambient light, but may not be necessary.

Our second prototype (Figure 3) therefore examines administering the text without a viewing box. It uses a small standing box to house the LED, diffuser, and microcontroller. The companion app and protocols are the same. Instead of placing their face against a viewing box, a person places the box on a flat surface at a height which aligns their eye to the light source. We conducted informal and exploratory testing in a room with normal light intensity (500-750 lux) and no visual distractions behind the box. In this testing, the box-free design obtained measurement results similar to those obtained with our viewing box prototype and the Lafayette system.

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[6] Part number: C503D-WAN-CCBEB151

[7] Part number: DG05-1500

[8] Part number: RFD22102

Discussion & Future Work

In addition to our continued work to refine hardware and test protocols, we have identified several questions we plan to investigate in future work. We believe these relate to broader questions in sensing and intervention for mental health, with our focus on CFF providing a perspective that complements work in other conditions.

First is *how to communicate results*. HE is a condition for which treatment is uncomfortable and inconvenient, which could potentially lead people to disbelieve results or even lie to a provider to avoid treatment. Should a system hide results from the patient, or require they connect with a health provider to interpret the results? Should a system provide instructions based on results? For example, if a result is below 39 Hz, should a system suggest the patient avoid driving and schedule an appointment with their provider as soon as possible? Hiding a result seems ethically questionable because it means withholding personal information from patients. Alerting a provider without a patient's consent may lead to ethical issues, but so might *not* communicating with a provider. Investigation with all stakeholders is necessary.

Another is *what factors may impact robustness and variance in measurements*. A major focus going forward will be in comparing the handheld prototype with viewing box designs, as well as examining the handheld prototype in different viewing conditions. A person's reaction time in identifying a threshold may be impacted by a motor impairment, a distraction, or some other situational impairment. Frequent self-administered testing will also provide new insight into how measurement are impacted by factors like fatigue.

A third is *how to design for long-term self-monitoring*. For example, in addition to supporting a person in self-administering a test, our proposed approach might be extended to provide guidance regarding when a person should take a measurement. This could go beyond population-based thresholds, using individual baselines and long-term self-monitoring to open new opportunities for personalizing management of chronic conditions like hepatic encephalopathy.

Our future research intends to work toward evaluating device performance, usability, and feasibility as a daily screening tool which can be self-administered by the patient in their home. We look forward to discussing various methodological, medical, and ethical challenges that arise due to nuances of the test. The UbiComp 2016 Workshop on Mental Health: Sensing & Intervention will provide an ideal venue for such discussion.

Acknowledgements

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