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Modeling Pharmacokinetics and Pharmacodynamics on a Mobile Device to Help Caffeine Users

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Abstract. We introduce a mobile device application that displays key information about caffeine: the pharmacokinetics (time course of drug levels) and pharmacodynamics (the effects of caffeine level) visually on the iPhone, iPod Touch, and iPad. This application, Caffeine Zone, is based on an existing model of caffeine physiology using user inputs, including caffeine dose, start time, and consumption speed. It calculates the caffeine load in a user for the next twenty-four hours and displays it using a line chart. In addition, it shows whether the user is currently in the "cognitive alert zone" (the range of caffeine where a normal person might benefit most from caffeine) or the "possible sleep zone" (the range of caffeine where sleep is presumed not affected by caffeine level.) Understanding the pharmacokinetics and pharmacodynamics of caffeine can help people using caffeine to improve alertness, including in operational environments. Caffeine Zone may also help users create a mental model of caffeine levels when the device is not available. We argue that this app will both teach users the complex absorption/elimination process of caffeine and help monitor users' daily caffeine usage. The model, with additional validation, can be part of a system that predict cognitive state of users and provide assistances in critical conditions.

Keywords: pharmacokinetics, pharmacodynamics, caffeine, mobile app, modeling

1 Introduction

Caffeine, the most widely used psychoactive substance [e.g., 1, 2], has long been regarded as an effective way to improve mental alertness and reactions, especially in critical operational environments like long-distance driving [e.g., 3], air traffic control, and nearly all operational military environments. Caffeine can be found in many different sources of foods, beverages, and medicines, including chewable gum in military rations. Some people take caffeine-contained substances, mainly coffee and tea, for well-being [2]; others for its pharmacological effects. Low to moderate doses of caffeine can indeed be very useful in military settings according to the National Academy's Institute of Medicine [4].

Overuse of caffeine, however, can impair cognition and health directly and indirectly. For example, higher levels of caffeine can lead to higher levels of cortisol [5]. Too

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much caffeine may disrupt sleep schedules[1] and may contribute to long-term chronic health issues such as agitation, anxiety [6], and insomnia. Users in stressful, high tempo situations might be particularly prone to using and overusing stimulants to maintain alertness (e.g., see a Naval Aerospace Medical Research Laboratory report [7]). Striking a balance between too much and too little is a challenging task because caffeine's use depends on understanding the pharmacokinetics of caffeine, because uptake and excretion are exponential processes, and because while the immediate benefit is during the task, the delayed response to eliminate caffeine may make users more sleep deprived later and over time. The computation and future impact of use may be beyond many of us to compute.

As a result, people who use caffeine for its pharmacological effects can end up with at least three possible problems. They can consume too little, and not be as alert as they need to be. They can consume too much at a single point in time and be jittery or have other side effects. Or they can consume a right amount but too close to when they would like to sleep and subsequently have trouble sleeping.

Before introducing an application to help users moderate their caffeine levels, we will briefly describe the caffeine model.

2 Understanding Non-linear Curves

We model two of the processes in the human body that modify the caffeine level: absorption and elimination. Absorption refers to caffeine being taken into bloodstream from its external form (liquid, tablet, gum, etc.). Elimination refers to caffeine being excreted from our body, mostly through urine. Both absorption and elimination rates are non-linear functions based on time. (We subsume distribution with absorption and metabolism with elimination.)

In our theory and in the software, we use the following equations taken from a review used for modeling caffeine in cognitive models and agents [8]:

$$\text{Caffeine absorption}_{t+1} = \text{Caffeine intake reservoir}_{t} * e^{-(1/7\text{min})} \qquad \textbf{(1)}$$

$$\text{Caffeine elimination}_{t+1} = \text{Caffeine in bloodstream}_{t} * e^{-(1/240\text{min})} \qquad \textbf{(2)}$$

That is, we have an absorption half-life of 7 minutes (eqn. 1) and an elimination half-life of 4 hours in (eqn. 2).

[1] The effect of caffeine on sleep varies. Some people are very sensitive to caffeine; some seem to have no sleep problems despite regular caffeine consumption in the evening [2].

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Soon after caffeine intake, the absorption and elimination processes start simultaneously: caffeine is being distributed into the bloodstream and excreted into urine. The exponential decay equations intertwined with one another may make it difficult for caffeine users to calculate the current caffeine intake in their bloodstream at any moment without external computation, and particularly difficult to predict the level in several hours when it will be time to sleep. This complexity is the major source of the aforementioned challenge—striking a balance of caffeine dose over time.

3 Caffeine Zone

Caffeine Zone is an application that utilizes the ubiquity and computational power of modern mobile devices such that an inexpensive and portable real-time caffeine intake can be displayed graphically. The current version of Caffeine Zone works on the iOS operating system—provided on iPhone, iPod Touch, and iPad—version 3.1.2 and above. There is, however, no conceivable reason it cannot be ported to other mobile devices such as the Android, BlackBerry, and similar devices.

3.1 Software Architecture

The software architecture of Caffeine Zone is shown in Figure 1, providing also an overview of the functions in the app. The application consists of three major components: main, history, and settings. The main component is where the formula are calculated and displayed; the history component is in charge of recording/managing the consumption history; the settings component is the center where settings are achieved and retrieved. The data points of caffeine intake are calculated for each minute and stored in the SQLite database that comes with iOS to save calculation time whenever the line plot is to be displayed.

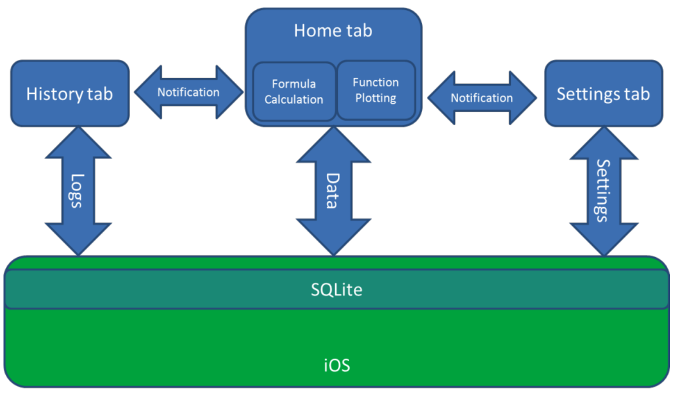

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Fig. 1. The software architecture of Caffeine Zone

3.2 The Pharmacokinetics Equations and Assumptions

We provide several parameters as defaults. These numbers are extracted from previous research in the pharmacology effects of caffeine. They are the half-life of absorption and excretion (currently implemented in the calculation and are unchangeable), and the thresholds for minimum optimal caffeine for cognition and maximum optimal caffeine for cognition. We also include a threshold for sleep. Weight is used to calculate dosage (dose by weight) and units to display, doses (mg), or dosages (mg/kg).

The minimum and maximums for the cognitive range are based on our review [8], and assume that the users are typical, which not all users are. These two numbers represent the minimal does of caffeine that can keep humans alert or that helps cognitive performance and the maximum dose of caffeine that does not impair cognition.

The half-lives are taken from our review. We know that the half-life of elimination should be moderated for nicotine users [9]. In general, the half-life for nicotine users is about half as long as for non-nicotine users. We intend to add this effect in a future revision. The threshold for sleep is currently taken from anecdotal reports by the developers.

These parameters will vary from person to person. Therefore, these parameters are adjustable—users can change the settings based on their usage.

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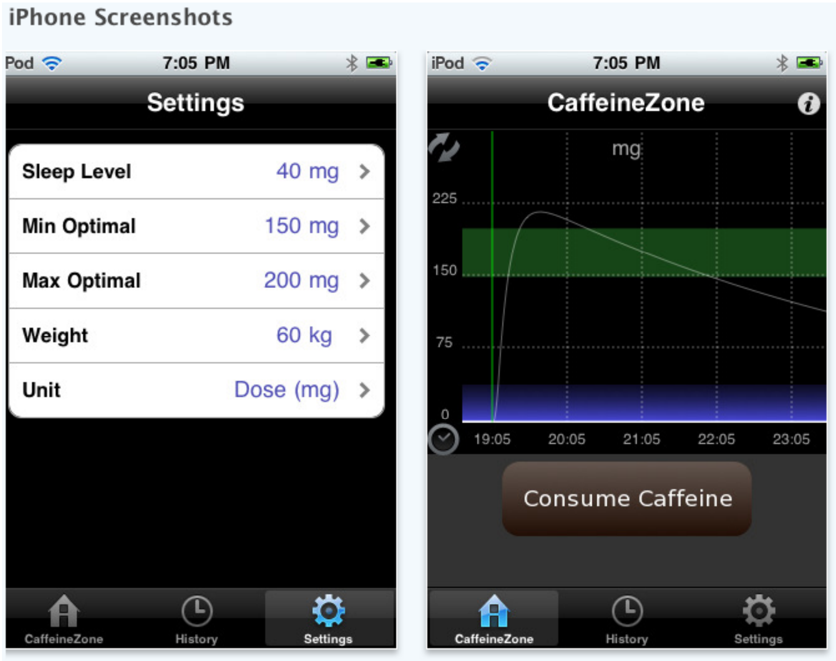

Fig. 2. The interface for Caffeine Zone, showing on the left some of the adjustable parameters, and on the right, the scrollable pharmacokinetics display.

3.3 The Displays

Figure 2 shows two of the current displays, including the timeline of caffeine. By displaying the caffeine model users can understand the time course of their caffeine levels, and moderate their caffeine consumption more effectively. For example, they can switch to decaf coffee before they have consumed too much and go above the cognitive alert zone, or stop consuming caffeine before they will have trouble sleeping that evening, and obtain coffee before they get into traffic.

The screenshot on the left of Figure 2 shows the settings screen where users adjust some thresholds and parameters. Changing the Sleeping Level, Max Optimal, and Min Optimal will change the range of the cognitive alert zone (green area on the right of Figure 2, 150 to 200 mg here) and the possible sleep zone (blue area on the right of Figure 2, approximately 0 to 40 mg here).

The screenshot on the right of Figure 2 shows the graphical plot of plasma caffeine concentration over a given time period on the main screen. In the screenshot, the user has consumed a dose of about 240 mg caffeine starting at 19:05. The plot area can be scrolled to left and right to cover forty hours of data points (twenty four hours before

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and after current point of time). The time on x-axis can be changed to clock time or canonical time.

3.4 Current State and Use

Currently, this application is distributed through the iTunes store as a free application. You can find it on iTunes by searching for 'Caffeine Zone'. Users can view more about it at http://www.caffeinezone.net, which includes information about the updates, features, and manual. We have had more than six hundred downloads from thirty-six different countries from August 2010 to January 2011.

3.5 Benefits of Caffeine Zone

This app may help operators create a mental model of caffeine and learn a better way to use caffeine as a psychoactive substance. Having a working knowledge of caffeine can reduce the risk of ineffective use of caffeine. Any operator wants to extend their cognitive attention or reduce reaction time may find this model of caffeine helpful.

In addition, an accurate model of caffeine can be used to predict when operators may loss their attention or become fatigue due to low caffeine load. Systems with the caffeine model will be able to predict users' cognitive state, or even emotional state, more accurately and provide assistance when needed.

4 Conclusions

We introduced a novel, yet readily accessible and inexpensive, way of visualizing caffeine intake for augmenting cognition through caffeine consumption for users. Because caffeine is already part of many people's daily diet, by using Caffeine Zone, users, including those in operational settings and safety critical systems, may be able to improve their vigilance and alertness and prolong cognitive attention more safely and with fewer side effects. There are many critical operational tasks, such as air traffic control, driving, and radar screen operators, that require constant alertness and heavy cognitive processes. Allowing these users to remain cognitively active in critical situations using and not over using caffeine may improve performance.

Caffeine Zone can be used as a caffeine monitoring device and a teaching tool for caffeine intake. Users who do not consume caffeine regularly can use it as a caffeine monitor—users with an iOS device now have a convenient and inexpensive real-time caffeine monitor to improve their cognitive alertness with the possibility of less over-use. Users who consume caffeine in certain pattern may build a mental model of

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caffeine that allows them to disengage from the tool but remain an effective caffeine consumer. Both types can learn from using this application and teach themselves without explicitly learning a complex model of caffeine. We suggest that this application will be eventually help caffeine users to improve their cognitive performance by more explicitly self-monitoring their caffeine use, and to learn how and when to use caffeine to improve their alertness and sleep pattern.

Understanding the effect of substances in cognition, such as caffeine, is a precursor of two interesting applications. One will be a more complex and complete system to model more than caffeine, perhaps sleep and other moderators of cognition.

The other interesting application is creating more sophisticated computational models of humans in synthetic environments. Including effects like those of caffeine helps modelers realize the limitation in cognition and adds another dimension or layer to the traditional theory of human information processing that deals primarily with an internal, static, and completely rational model of cognition.

4.1 Limitations

There are several limitations to Caffeine Zone. These range from limitations to the theory to limitations of understanding the application's use and impact. Limitation with the equations: There is no consensus of a complete caffeine model to the best of our knowledge. Our model is based on our own search in this area, and we are aware that the parameters might vary for different populations and different environments (e.g., [10, 11]). The adjustable thresholds can mitigate part of this limitation, however.

Limitations with the interface: Our app does not include a rich set of caffeinated beverages and foods. More and more energy drinks include substantial amounts of caffeine. Including these would make the app easier to use. In addition, there are some inherent limitations in these numbers because there are variations in the amount of caffeine in the same type of beverage, for example, in coffees. Although there is a custom option when entering data to our app, using it may require more knowledge about caffeine levels in different substances than a novice user might have. For example, to know the amount of caffeine in a 30 oz. coffee will require the caffeine/ounce and then a multiplication. Providing an extensive set of predefined sources of caffeine will make data entry easier, faster, and less cognitively demanding for many users. To achieve this, we should include a more complete database of caffeine content in foods and drinks.

Limitations with impact: in this case, we do not know if and how it is used: As it stands today, there is not enough empirical data to support our conjuncture that users will often use and learn from our app as we expect they will. In fact, the history has taught us that people will use a technological tool differently than what the original

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designers expect. One local Caffeine Zone user told us he used it to "coach" him when to consume to remain alert at a specific time period in the future. We are planning to start collecting preliminary data to learn how such feedback works and to understand its impact to regular users.

Finally, it is not used enough to have a broad impact. There is only a small user base for this application, and we have not collected empirical data to see whether the current users do benefit from what we think they will. We need more users and feedback to analyze and maximize it impact and validate our absorption and elimination formulas.

4.2 Future Applications

Further work on this application is possible, including both near term and far term projects. In the near term, we will work on the area of extending the application to help coach users, that is, to generate a recommendation on when/how much to drink, given different goals such as to remain alert during a period of time, not being influenced by caffeine at certain time, etc. This will mean including a set of alarms to know when to start or stop consuming based on user-defined thresholds.

In particular, we are working on a revision that will include three alarms/guards to help users regulate caffeine consumption: (a) a Min alarm: this alarm generates a notification when the caffeine intake is about to drop out of the cognitive alert zone. Users can use this notification and decide whether additional caffeine consumption is appropriate; (b) Max guard: this guard pops up a warning when the app detects the consumption of the caffeine source will generate a caffeine intake that exceeds the maximal threshold. This function allows users to change the amount/way they are about to consume caffeine. (c) Sleep guard: this guard pops up a warning when the app detects that the consumption may interfere with sleep. Again, this function will allow users to change their behavior immediately.

Users might also be able to apply this application to different but similar drugs and substances. When the half-lives of absorption and eliminate are modifiable, other drugs can be modeled, and the platform can be used for teaching about other drugs, including nicotine, for example. This will extend the potential use of this app to a broader audience.

We are also starting a study to understand whether and how people change their use of caffeine based on this application. This may provide evidence about how Caffeine Zone alters the use of caffeine, and may provide additional feedback about how the app is used and can be improved. In addition, we would like to study the use of Caffeine Zone by different types of users. So far, we have studied users pretty much like ourselves. It would be useful to see how it is used by users on ships or in a

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desert, and in operational environments were ease of use might become acute, or where sleep cycles change, or where caffeine sources vary.

Longer term, we could extend this approach to include more aspects of behavior and the environment that affect alertness. These factors could include physical activity and previous rest, time of day, and other foods known to influence alertness. The app could also measure alertness directly and modify the equations accordingly for each user. If there are mobile sensors that can provide psychological information such as heart beats, blood pressure, and pupil dilation, incorporating these information with the caffeine model will provide accurate cognitive state measurement data for augmented cognitive systems.

Finally, this work may be useful inside other systems trying to predict and assist users. From a designer's point of view, a system should have a model of the user to assist understanding and predicting its users. If the users are tired or fatigued and use caffeine, the system could create visual or audio cues or offload cognitive intensive process to automation or other team members. This could help prevent errors. Our caffeine model can be used with other cognitive state measurements to provide a more accurate user model to help augment cognition and performance.

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