COGS 209 Mini-Project Proposal

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Title: Development of a chemotyping strategy for consumer *Cannabis sativa*

Research Question

Cannabis is the third most commonly used substance worldwide with approximately 18% of Americans having used it at least once in their lifetime (Substance Abuse and Mental Health Services Administration, 2020). Out of these users, 10% report using cannabis for medical purposes (Compton et al., 2017). Cannabis has been approved for medicinal use by the US Food and Drug Administration (FDA) for various conditions such as chemotherapy-induced nausea, unattended weight loss caused by HIV, and for chronic pain management (Hill, 2019). However, research on *Cannabis sativa* has long lagged behind the boom in consumer access to cannabis. This may be influenced by the US Drug Enforcement Administration ruling cannabis a schedule I drug in the 1970s, increasing barriers to access the drug for many basic science laboratories. Additionally, until 2022, the only NIDA-approved government cannabis supplier was at the University of Mississippi (US Food and Drug Administration, 2023). This supply lacked the potent concentration of relevant cannabinoids that many Americans can find at their local dispensary, particularly as consumer trends push cannabis products' potencies to even higher levels than previous decades (Chandra et al., 2019).

Furthermore, it has been demonstrated *in vitro* that of the 200+ phytocannabinoids and terpenoids naturally found in cannabis, several interact with the endogenous cannabinoid receptors (Dvorakova et al., 2022; Straiker et al., 2021). Therefore, the various compounds found in cannabis may interact at the receptor and produce a synergistic "entourage effect" (Russo, 2011). Altogether, this evidence suggests that compounds other than Δ^9-THC may contribute to the psychoactive and medicinal effects of cannabis. For example, cannabidiol (CBD) has recently been shown to exhibit anti-inflammatory, anti-epileptic, analgesic, and neuroprotective properties (Gonçalves, 2020). Currently, the cannabis industry standard is to classify strains by species (*indica*, *sativa*, *ruderalis*), but with widespread cultivation, genetic modifications, and unstandardized testing protocols, chemical makeup is relatively uncorrelated with species (Smith et al., 2022; Jikomes & Zoorob, 2018). Therefore, it would be more accurate and beneficial to the consumer to classify strains by chemical makeup alone.

Data/Materials.

We will use a publicly available cannabis chemical profile data set used in the article by Smith et al. (2022) entitled "The phytochemical diversity of commercial cannabis in the United States"

(https://doi.org/10.1371/journal.pone.0267498) maintained in a github-hosted csv located at: https://raw.githubusercontent.com/cjsmith015/phytochemical-diversity-cannabis/main/data/preproc_lab_data_pub_20220218.csv\

We have decided to compare ratios of cannabinoids and terpenes between samples rather than their absolute masses in order to account for variation due to product type (i.e. flower product vs concentrate product).

Course impact/relevance.

In order to create meaningful, chemically informed categories with which to classify cannabis, we will perform a cluster analysis after using dimensionality reduction on the normalized data set. Once our data has been assigned to clusters, a classifier could be trained and tested on separate subsets of the data to determine which chemical constituents are most important for categorizing cannabis.

Outcomes.

One result of the analysis will be a set of cannabis categories based on chemical similarity. Clusters can be further characterized through analysis of the means and variances of the cannabinoid and terpenoid profiles of the strains that comprise them. Another potential result is a classifier capable of categorizing new strains into the newly generated categories.

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