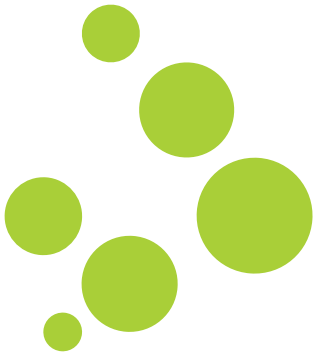
STEM Games 2019



Science

HIJACKING THE BRAIN

designed by

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Day 1 - Structural chemistry

During a routine airport check, Croatian police have arrested a group of students carrying a crystalline powdered substance named *STEM* (Synthetic Turbo Excitatory Molecule). Since *STEM* failed routine drug tests, it was seized by narcotics agents as a suspicious item. *STEM* was suspected to be a prohibited substance, and was sent to the National Forensic Service for forensic identification.

The group in which you are working at the National Forensic Service is focused on determination of the chemical structure, biological activity and behavioral effect of newly synthesized drugs discovered by the police. In order to investigate the structure of *STEM*, you have performed liquid chromatography-time-of-flight-mass spectrometry, and 1D and 2D nuclear magnetic resonance spectroscopy. Results of the *STEM* tests are shown below.

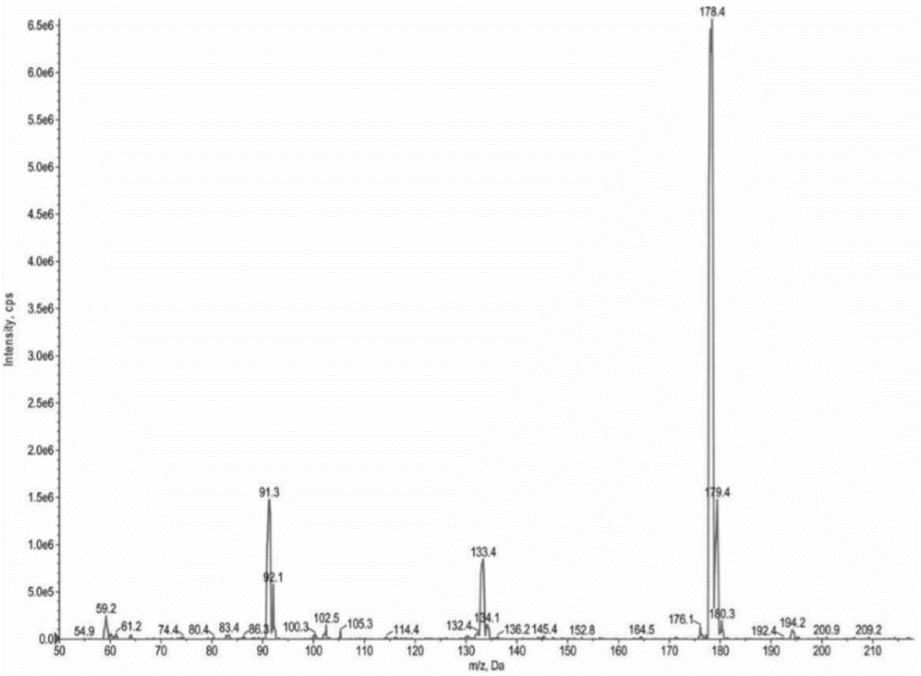

Figure 1: LC-MS-MS

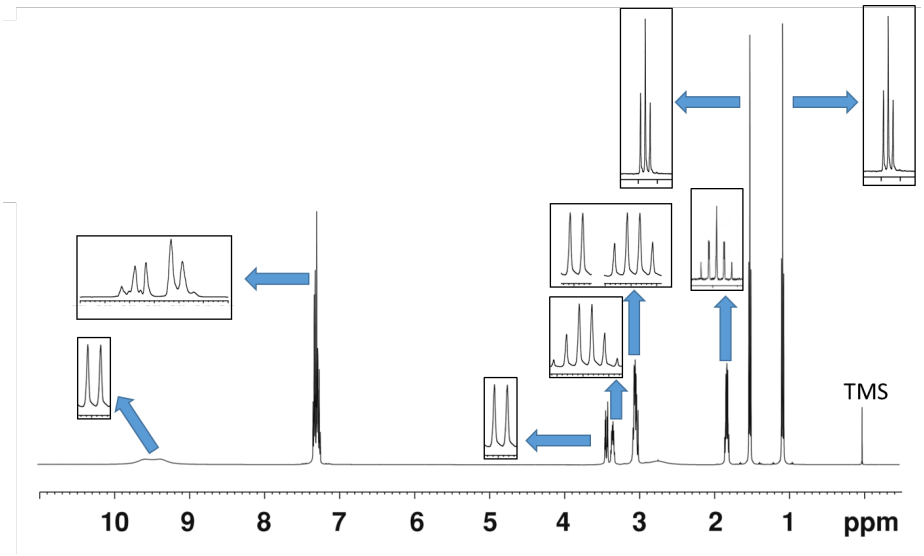

Figure 2: $1D - H^1$ NMR

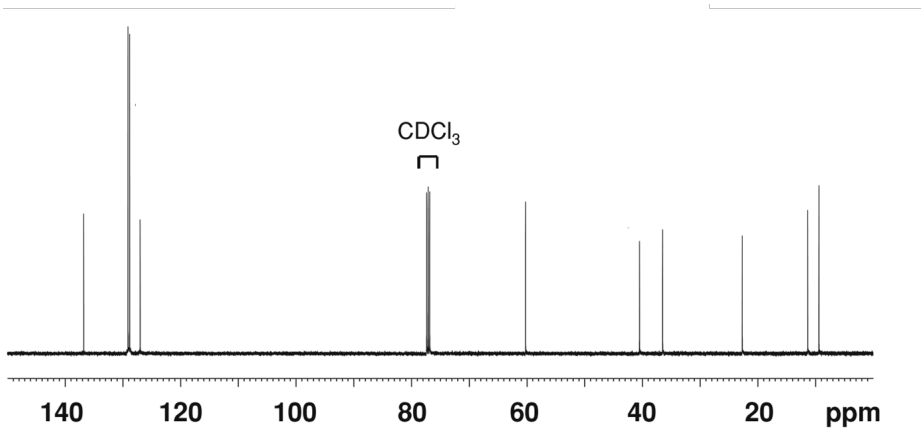

Figure 3: $1D - C^{13}$ NMR

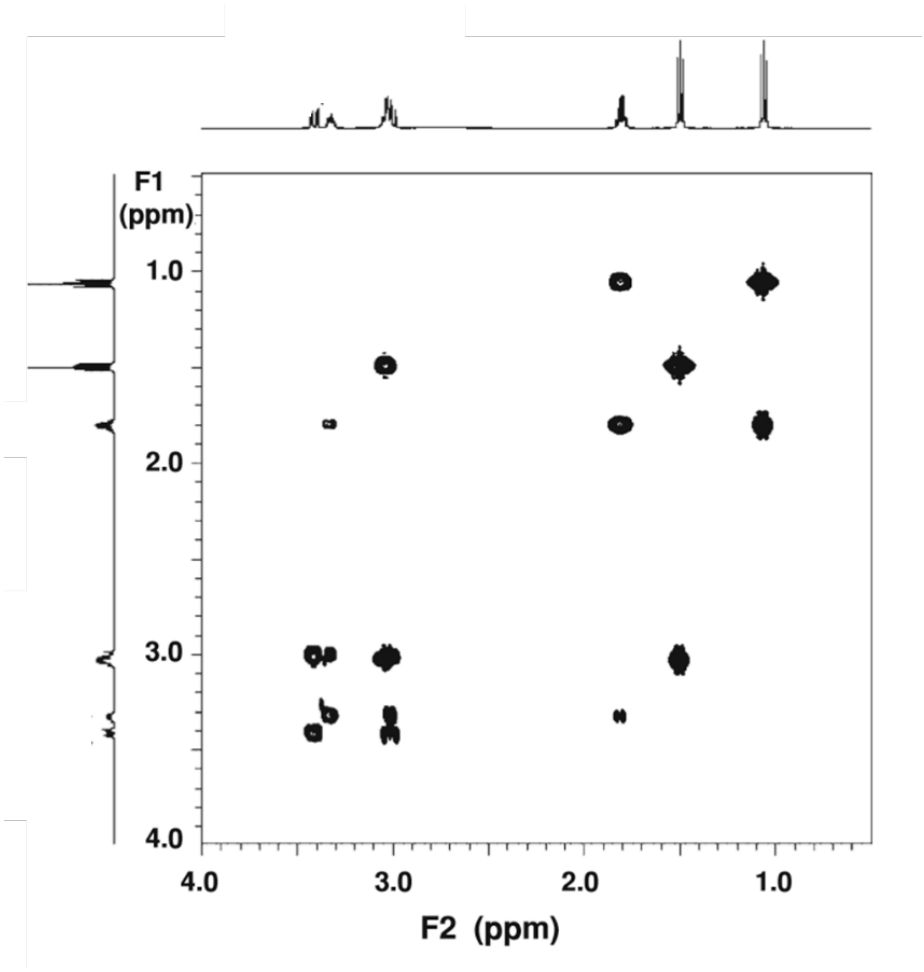

Figure 4: $2D - H^1 - H^1$ COSY

Task

Based on the data provided explain the following:

A) How did you use each of the methods to identify parts of the structure of *STEM*?

B) What information did you obtain from the LC-MS-MS spectra?

C) What information did you obtain from the 1D and 2D NMR data?

D) The exact *STEM* molecular formula.

E) The relative molecular mass of *STEM*.

F) The exact chemical structure of *STEM*.

G) The IUPAC name for *STEM*.

H) How can *STEM* be assigned to a drug group based on its structure?

Day 2 - Behavioral neuroscience

Although *STEM* has now been successfully identified, its narcotic effects remain unknown. Your group believes that there is a possibility for *STEM* to become a widely abused for recreational use in the near future, and therefore you will start to test the effects of *STEM* using an animal model. Since your group is on the low budget, the only available animal model that you can use is *Drosophila melanogaster* (the fruit fly).

From the preliminary toxicology results you know that, depending on its concentration, *STEM* can cause a series of behaviors such as cleaning of wings and proboscis, increase in locomotion, buzzing, twirling, unconsciousness and even death. In order to test which genes and proteins are involved in the development of these behaviors, your group should develop two behavioral assays. The first assay will give you information on **D**ose **D**ependent **R**esponse (**DDR**), where flies are exposed to the drug by a researcher, and the second will enable testing features of addiction where flies can **C**hoose **B**etween a **D**rug and a **N**on-**D**rug (**CBD/ND**) source.

Task

A) **DDR** behavior assay.

1. Which type of behavior (from preliminary toxicology results) would you use to perform **DDR** on flies using *STEM*?
2. How would you quantify that behavior in the **DDR** assay?
3. In order to perform high-throughput analysis of isolated **DDR** behaviors, all flies in the cohort should be administered with the *STEM* at the same time. Which drug administration technique would you use and way?
4. Provide a short scheme and description of the **DDR** behavior assay with all controls groups, possible obstacles and its potential future applications!

B) **CBD/NB** behavior assay.

1. Provide a short description and scheme of the **CBD/ND** assay, applicable for use with *Drosophila melanogaster* with all controls groups.
2. How would you quantify the amounts of drug and non-drug source consumed by the flies during the assay?
3. In order to test if flies will self-administer the drug even when it has negative consequences, propose a method of punishment will you introduce as a deterrent to selecting the drug?
4. What information can you get from **CBD/ND** that can be compared to the **DDR** behavior assay?

Day 3 - Molecular biology

After testing *STEM* on wild type flies using the **DDR** and **CBD/ND** assays, your group discovered that the flies respond to the *STEM* in a dose dependent way, and that flies, when given a choice, prefer food containing *STEM* compare to regular food. Like other drugs from the same group, *STEM* can induce addiction, and therefore it is important to determine the molecular mechanism of action of *STEM*. To identify which genes and proteins are involved in acute response to *STEM*, you will perform a series of tests on mutant and transgenic flies using your developed DDR assay. To speed up the gathering of preliminary results on *STEM*'s chemical structure, biological activity and effects on behavior, you will be focusing on its effects only on the presynaptic neurons of the fly brain.

Task

A) Based on the structure of *STEM*, suggest at least two protein targets in presynaptic neurons that could be affected by *STEM* administration.

B) Which techniques for genetic manipulation, commonly used in flies, will you use in order to test these potential protein targets of *STEM* (two protein targets chosen in the first question)? Provide brief scheme of the method(s).

C) Which behavioral results can you expect in the **DDR** assay if the chosen proteins are involved in the acute response to *STEM* administration? What results would you expect if they are not?

D) How can you separate the influence of *STEM* on these chosen proteins in dopaminergic neurons, from effects on other neurons of the fly brain? Provide brief scheme of the method(s).

E) Propose genetic manipulation technique(s) that you can use as tool(s) for silencing neuronal transmission in specific neurons or brain regions. Provide brief scheme of the method(s).

F) Which behavioral results can you expect in the **DDR** assay if the specific neurons or brain regions where silencing occurred are indeed involved in *STEM* molecular mechanism?

G) In order to mimic the influence of *STEM* on the fly's behavior, you can activate neuronal transmission. How can you do this and how would you interpret your results comparing to the effect of *STEM* on wild type flies? Provide brief schemes of the method(s).