Medicinal Chemistry Research Coursework

Faculty: Natural Sciences

Department: Chemistry

Module name: Medicinal Chemistry 2

Degree: BSc Chemistry, MSci Chemistry with Medicinal Chemistry

Level: Y2

Approximate number of students: 60-80

Duration: Set over 4 weeks, expecting 10-15 hours of work from students

Weighting and credit: 20% of module, module is 8.3% of Y2, Y2 is 20/35% of BSc/ MSci degree respectively

Module ECTS: 5

Module Type: Elective

Insights colour key

Educational Developer

Inclusivity

Learning Designer

Registry

Careers

Assessment overview

The medicinal chemistry research assessment is an individual written coursework in a question-and-answer format, exploring the questions medicinal chemists might consider when selecting a drug target and investigating potential drugs. Assigned in Year 2 towards the end of Spring Term, it also practices use literature to explore the topics that might be covered in a journal-style introduction and allows for some creativity in the use of a software called PyMOL to visualise the binding interactions between a potential drug and a drug candidate.

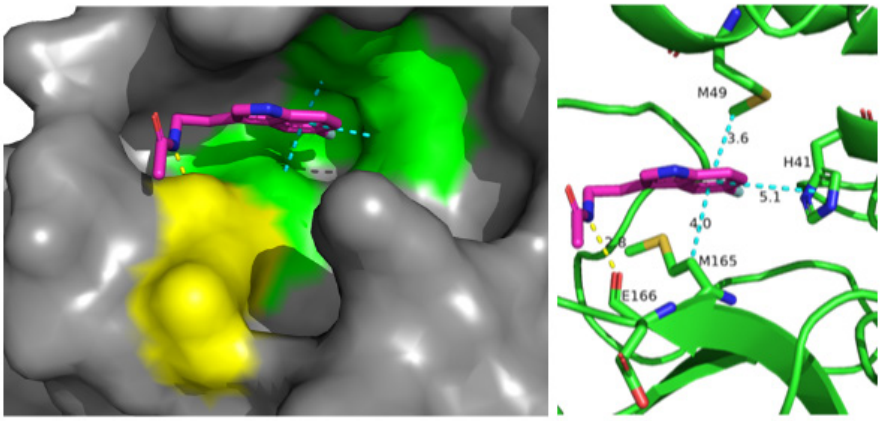

Figure 1: An example of images generated using the PyMOL software, to visualise the binding of a potential drug (magenta) to its target.

PyMOL is specialist software available which is used for visualising molecules. It is available via the Imperial College Software Hub.

Design decisions

Rationale and Design

This assessment is designed as an assignment that draws on some of the work medicinal chemistry researchers might perform during a PhD or Industry project. The questions prompt students to consider concepts they would likely have to consider when working on a drug target. Medicinal chemistry is a subject which can involve a lot of memorisation, and this assessment aims to combat that by incorporating a 'learn-by-doing' methodology that mimics real-world medicinal chemistry research.

Designing tasks that imitate what students might be doing going into the industry aligns well with authentic assessment as it provides students with an opportunity to produce a piece of work that has meaning and value beyond the purposes of the assessment itself. This may lead to better engagement with the topic and better learning.

Part 1 of the assessment features questions that centre on the choice of drug target and methods to identify potential drugs. This is designed as an opportunity for students to practice literature searching, formal writing, and to understand what is required in a journal-style introduction. The total

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word limit for the coursework is 1500 words (±10%), which aims to encourage students to write succinctly. This is a key skill for research work and exam technique, as well as preventing students or markers committing too much time to the assessment. Please see below for sample questions for Part 1.

TASK 1 Questions!

i) Briefly explain why research to develop anti-viral drugs against SARS-CoV-2, alongside research into vaccines and antibody therapies, is relevant *(4 marks)*

ii) M^{pro} is a cysteine protease. Using a schematic of the likely reaction mechanism of the protease, explain the proposed catalytic mechanism ensuring you include the key amino acids that are proposed to be involved in the process. *(4 marks)*

iii) Using PyMol and the unliganded structure (PDB ID 6y2e), generate an image showing the active site of the enzyme clearly and identify the sub-sites. *(4 marks)*

iv) Explain why you think M^{pro} is a relevant and good target for COVID-19 drug discovery, using evidence from the literature to support your answer. Examples of ideas you might want to consider here include but are not limited to: functional role of the protein, its structure, selectivity for virus/host, feasibility.... *(10 marks)*

v) Are there any challenges about M^{pro} as a target that should be considered by researchers? *(4 marks)*

Use your knowledge from lectures and the literature to help you and cite sources to support your answers.

Figure 2: These questions form Part 1 of the assessment and focus on literature research of concepts which might be covered in the introduction to a paper.

The literature searching and aspects of write up could be difficult for students with dyslexia or specific learning difficulties. The reason for it are the difficulties with controlling the flow of information. When working with a bigger number of sources it can be difficult to structure the writing. This is where tools such as concept matrix alongside a visual spacial plan can be useful. Traditionally, students wanting or needing support from the disability office would be supported in isolation, however, integrating those tools into the broader module level teaching can be also beneficial to other students.

Part 2 of the assessment involves students using the binding visualisation software PyMOL, using the images they generate to describe the binding of drug fragments to a protein target and to propose how to develop the component further. This was designed to enable students to visualise the largely theoretical concept of drug-target binding, and whilst students may not use the software in their own work, it includes some creativity in the coursework, aiming to avoid it being too 'dry' and enhancing student engagement.

TASK 2 QUESTIONS!

i) The authors of this research decided to take a fragment-based approach to finding M^{pro} inhibitors. Why did they decide to take this approach? *(4 marks)*

ii) Pick **three** of the above ligands and for each of them use **PyMol** to analyse their binding interactions. For example, do they form hydrogen bonds to particular amino acids in the binding site, is there filling of a hydrophobic pocket etc...

In your written report you should explain what you have observed and include appropriate figure(s) showing the ligand binding, key amino acids involved in interactions with the ligand, and appropriate labelling of the key protein residues. *(12 marks)*

Figure 3: An excerpt from Part 2, which asks students to use the PyMOL software to analyse binding interactions.

The Q&A format was chosen to give students a highly structured way to explore the literature and guide them to what information and concepts they should be paying attention to. Sticking to a written assessment was important for students to get feedback on their written work as preparation for the full lab report assessments in Year 3. It also allows for a deeper exploration of ideas than, for instance, a poster assessment might. It also maintains the variety of assessment types, as a poster presentation is one of the Year 2 module assessments.

This is an individual assignment, mainly to give students a chance to work independently since other modules (Chemistry of Molecular Systems; Macromolecules and Materials; iEngage) include group assessments towards the end of Year 2 Summer Term.

Alignment with Learning Outcomes

The learning outcomes (LOs) that this coursework is most aligned with are:

- Explaining and evaluating methods for lead compound identification and optimisation including rational drug design
- Critically analysing binding of small-molecule drugs
- Comparing different biological targets

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Literature searching is another skill this coursework seeks to develop and assess, and is necessary for students to achieve the higher grades. However, the questions are designed such that a passing grade could be obtained based only on a thorough understanding of lecture content. Given the weighting of the questions if no literature at all consulted could probably still get a low-middle 2:1. Not using the literature would definitely be a limit for accessing the first class bands.

Fit with other assessments in the module and the programme

This assessment is delivered towards the end of Spring Term in Year 2. It builds on a similar question-and-answer assessment from Year 1, in which students are given one paper on a drug development project to read and use to answer short-answer questions, as a more-structured version of Part 1 of the Year 2 assessment. In preparation for this Year 1 assessment, students are also given a short video lecture breaking down the parts of an introduction from an example literature paper to show how the authors cover the existing literature and the new work communicated in the paper. To prepare students for Part 2 of the Year 2 assessment, there is formative feedback from a Year 2 Autumn Term task on identifying molecular interactions and a specific workshop on Pymol in term 1. Watch this video on the disadvantages of formative assessments.

In Year 3, students are asked to write full lab reports with in-depth introductions for the first time. The introduction is often a weaker aspect of these first Year 3 reports. Part 1 of this Year 2 assessment aims to prepare students for this, so they enter Year 3 well-equipped with an understanding of what is expected of them in an introduction. The questions in Part 1 therefore form a scaffold for ideas that would be covered in an introduction to a paper on the drug target and are heavily literature-based. Since Year 2 students are not yet expected to be able to write a full introduction, the Q&A format is used as a stepping-stone towards the full introduction expected in Year 3. Similarly, suggested search terms are given to help students start their literature search, as searching the literature for the first time can be quite intimidating.

Since this assessment involves literature research, it was placed towards the end of term 2, to closely follow the library training students attended on how to read a paper as part of a transferable skills module, iEngage. Literature research and writing are of course very broad skills and come up a lot throughout the course. The closest instance to this assessment in terms of the skills is the multiple group assignments in other modules (Chemistry of Molecular Systems; Macromolecules and Materials; iEngage) at the end of Summer Term in Year 2 which require literature research skills, for which the slightly guided literature research in this individual assessment prepares students.

Using the PyMOL software is a specific skill but may come up in future courses depending on students' Year 3 module choices or BSc/MSci project. However, the visualisation should benefit to students' understanding of drug-target binding for the remaining Year 2 module assessment.

Assessment design that allows students to build up the necessary skills that they can take forward can facilitate student learning. The main consideration is to ensure that the same task is not (in effect) assessed twice as part of a different module at a later stage; the nature and purpose of each assessment at each stage has to be sufficiently discrete to ensure that students are building / progressing on what they have done previously and not simply replicating it.

Practicalities

Preparing students for assessment

Two optional, one-hour drop-in sessions were hosted on Teams, with one member of staff fielding questions from students. They were held in the first and third week of the assessment period. These were relatively popular with students and helped solve some queries that might have been difficult to answer via Blackboard Discussion Board.

Offering additional scaffolding in the form of drop in sessions is excellent practice when it comes to assessment preparation. This in combination with discussion boards gives the students a variety of channels to engage and seek support as they work through the assignment. Having 2 drop in sessions at different points prior to submission also creates an incentive to start working earlier.

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It was estimated for students to spend 10-15 hours on this assessment. This duration was chosen considering that students have multiple other modules running in parallel to this one, and the weighting for this assessment was then chosen on the basis that it required about 15 hours of work. It is suspected that the average time students spent was over 15 hours, in which case it will be necessary to reflect on how realistic the timing is, and either accommodate for a longer assessment time (e.g. more weeks to complete the assessment, and/or increasing the assessment weighting), or shorten the assessment slightly and communicate the expected timing to students more clearly. In this case, the expected 15 hours of work was only communicated to students in the drop-in sessions, and adding it to the Blackboard page for the coursework could encourage students to spend closer to the expected hours on the assessment.

It is a really good practice to have in mind, and give students' guidance on, how many hours they should spend on the assignment. This should be communicated clearly from the start via different channels to keep the students to manage their expectations and appropriately direct their learning efforts.

Implementation

The first year this assessment was offered, it took roughly a week of solid work to design. This included aligning it to module learning outcomes and lecture content to find key points for the assessment to link to, as well as choosing a live, active research project to use to guide it that had appropriate publicly available data, writing and selecting questions, and making the mark schemes.

To refine the questions, the assessment was looked at from a student perspective, to see what search terms students might use, and what the literature results would be. This led to cutting questions that didn't have accessible answers in literature. In addition, the dataset of crystal structures from the publicly available dataset had to be cut down, selecting those with enough interesting binding elements to discuss without being too complex. This meant the assessment designer selected 6 from the roughly 60 available, from which students then choose 3 to analyse in-depth.

The second year of implementation involved some time for iteration, but of course significantly less than in the first year. In the future, an area of improvement could be allowing for extra time to be allocated for any significant change in topic. As the research project on which the coursework is based moves on and the literature changes, this is likely to be needed.

Two one-hour drop-in sessions were held to help advise students, and a discussion board hosted on Blackboard which required relatively little time investment from the host. The main time commitment for staff lies in the marking and feedback provision – this led to the feedback release date being moved back in the 2021-22 year, as the time commitment had been underestimated, as well as moving the submission date forward to avoid clash with other assessments and also ensure the feedback could be turned around in time before exams

Feedback and Marking

This assessment was marked by an individual member of academic staff, with check marking, so avoided the challenges posed by spreading marking across a team of academic staff of GTAs. However, in principle marking could be split. It should be noted that this style of assessment takes a relatively long time to mark, with each script taking at least 30 minutes. This led to the submission date being moved forward from the original timeline, to allow time for a good standard of marking and feedback whilst still returning feedback in time for the summer exam. Marking was done question-by-question to make it as fair and efficient as possible.

One focus throughout the module design was to allow for feedback throughout, instead of only providing feedback at the end of the year, so that students can use previous feedback for the next module assessment. For instance, the Year 2 Autumn Term molecular interactions assessment feedback was designed to be useful for this Year 2 Spring Term coursework, and the feedback from this coursework was designed to apply to future lab reports as well as the Year 2 Summer Exam for the module.

Having a well designed feedback strategy for the module and the programme creates better conditions for students to make use of feedback. The feed forward properties that are discussed...

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...here (where there is some indication of how comments from the current assignment can help in future learning on other modules) creates a greater need to acknowledge feedback and its importance. Having an overall feedback strategy also helps to connect feedback events across the modules and programmes creating a more holistic learning experience for the students and allowing for opportunities to better develop students' feedback literacy.

Whole-cohort feedback was also provided, as a written Word document in the Coursework Blackboard folder. Other assessments in this module use the platform 'padlet' for formative assessment feedback while allowing students to learn from each other's work, as well as video feedback which can be more personal and engaging for students, as well as helping staff to communicate a topic slightly differently to how they would in a written format. An additional benefit to video feedback is that it is not as easily transferrable between year groups as written feedback.

Video feedback has been found to be an effective way to deliver richer, more detailed feedback that better supports student learning (Mahoney, 2019) than its written equivalent. This is because it provides additional cues in the form of the tone and intonation that can alter interpretation and meaning. There is some evidence that suggests that lecturers giving video feedback include more praise than those providing written feedback (Mahoney, 2019) so it's important to ensure that the feedback is balanced. This resource provides more guidance on how to give video feedback.

Note that Padlet is not College supported so while this may work well it may be worth considering College support alternatives for providing formative feedback.

Advantages of the assessment type

- Stimulating to develop as directly interacting with current research projects and literature
- Scope for students to demonstrate different strengths compared to the exam
- Focus on application of knowledge; greater authenticity
- Timing provides feedback to me for remaining teaching
- Feedforward qualities of feedback making it useful for subsequent learning creating a bigger need to make use of feedback

Limitations of the assessment type

- Linking to live research creates risk of rapidly becoming outdated; regular revision required
- Not easily scalable without increased staffing
- Recent student data suggest that there is a breadth of time being spent on the assessment, with a few individuals spending almost 4 times as long as the upper recommended time (15 hours). Some further exploration of why students were spending this length of time is needed.
- Monitoring/understanding impact on student workload can be challenging

Advice for implementation

- Give students a guide on time required; seek feedback from them on time actually spent to help gauge if expectations are accurate.
- Plan in marking time into workload consideration for staff from the start.
- Good awareness of wider curriculum structure helps in focusing relevance and helping demonstrate benefits to students of wider skills and feedback.
- Use College supported educational tools to get maximum support with implementation and troubleshooting. Your Faculty Ed Tech team can advise on that.
- Offer additional support during the time that students are supposed to be working on the assignment. This might also help student to distribute their workload appropriately and manage their time better to monopolise on this extra support.
- Provide suggestions of organisational tools that help with making sense of literature search. This might benefit all students but will be particularly useful for students with specific learning needs who might struggle with organising information from different sources.

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