Australian Government

ANSTO

Proposal writing

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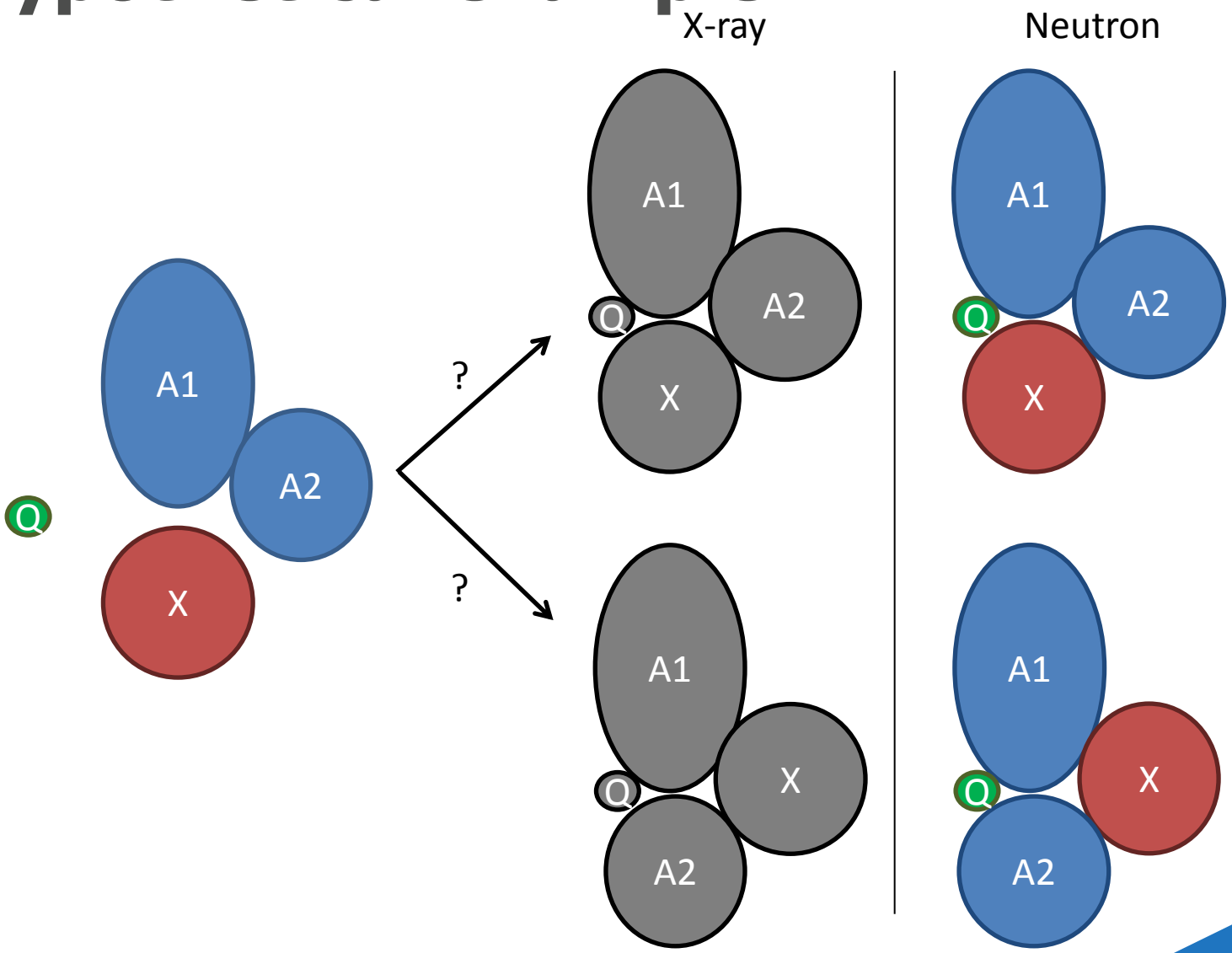
Science. Ingenuity. Sustainability.

A hypothetical example

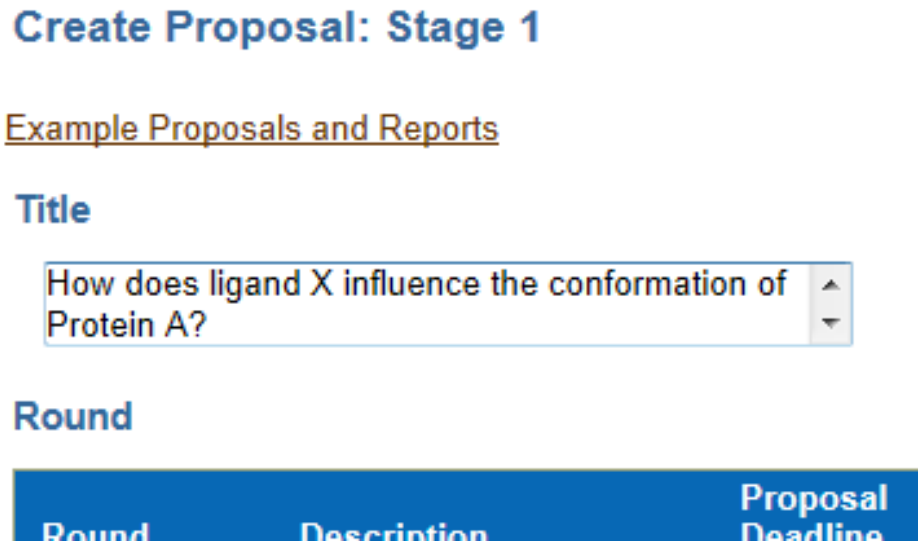


The ACNS Portal (neutron.nbi.ansto.gov.au)

- Experiment
- Researchers
- Instruments
- Samples
- Figures

Proposal Title

- Try to avoid generic titles
- Specific titles help to differentiate related proposals
- Titles posing a question can sometimes help to keep the reviewer focused
- Can be changed at any point before submission



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Proposal Details

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Proposed Research (Text)

Your proposed experiment should provide the following information:

- scientific background,
- aim of the proposed experiment,
- detailed description of experiment (remember that referees might not be experts in the field),
- results of preliminary work carried out (e.g. using x-rays, NMR, etc.)
- reason for choice of requested instrument,
- indicate how you calculate the requested beam time (depending on number of samples, and sample-environment conditions such as temperature, etc. for each sample),
- provide an overview of how the data will be analysed,
- list relevant published literature.

Maximum 800 words.

***** I advise uploading a 2 page PDF *****

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Scientific Background (The What)

- Allow about 3-4 paragraphs (½ - ¾ of a page)
- You need to clearly state:
  1. General background and relevance of the area of research (reference seminal work and reviews)

e.g. Cellular signalling is a complicated process regulating and coordinating the myriad of processes in the cell in response to a variety of factors. Dysfunction in the signalling pathways in cells can cause diseases such as …. [ref]. These diseases place a burden of approximately $ X billion per year on the health system in Australia, and this sum is projected to double in the next decade [ref].

Scientific Background (The What)

- Allow about 3-4 paragraphs (½ - ¾ of a page)
- You need to clearly state:
  2. The background and importance of the system being studied (reference closely related work)

e.g. ABCDs are a class of protein (~70kDa) involved in regulating … [ref]. These proteins have a variety of binding partners that modulate their function. X is one such binding partner (~30kDa), that prevents binding of ABCDs to their target in response to … [ref]. In some individuals the ABCD:X interactions are linked with a range of chronic diseases [ref].

Scientific Background (The What)

- Allow about 3-4 paragraphs (½ - ¾ of a page)
- You need to clearly state:
  3. Outline your specific research and motivation (if possible reference work from you own research group)

e.g. Protein A (an ABCD protein) and its ligand X has been linked to … in … individuals [ref]. There are a number of schools of thought on the issue of dysfunction caused by Protein A:X interactions. Our research group has evidence that when Protein A interacts with X, a small molecule, Q, can bind irreversibly [ref] (Fig. 1). We intend to better understand the molecular details of the ProteinA:X binding in order to develop strategies to prevent and treat …

Aim of the Experiment (The Why)

- In my view, the best way to frame the aim is through a testable hypothesis and a statement of the test

  e.g. We believe that binding of X induces a large conformational change in Protein A that exposes a binding area for Q. To test whether ligand X induces a large scale conformational change in Protein A, we propose a small-angle neutron scattering experiments with contrast variation to determine the low-resolution structure of Protein A with X

- However, you could also write a direct statement of the aim of the experiment

  e.g. The aim of the experiment is to determine the structure of the protein A:X complex using small angle scattering with contrast variation

Experimental Details (The How)

1. Clearly describe your experimental approach, including relevant details such as size, scattering length densities or match points, isotopic labelling

   e.g. To accurately determine the nature of any structural rearrangements in Protein-A upon binding to X, we propose a small-angle neutron contrast variation experiment. X is a 30kDa protein that will be deuterated to the 75% level, such that it is contrast matched in ~100% D_2O. Unlabelled Protein-A (70kDa, with a match point of ~40% D_2O) will be complexed with ^{D}X, and small-angle neutron contrast variation data will be measured at a range of D_2O concentrations including the two stated match points (Fig 2A). This data should allow us to determine the structure of both Protein-A and X in the complex.

Experimental Details (The How)

2. Clearly describe your experimental configuration including sample concentration, temperature, required q-range, time justification (here we also include some preliminary data)

   e.g. *We routinely prepare this complex at concentrations of 10mg/mL, however, preliminary SAXS studies suggest that there is a measurable structure factor above 5mg/mL (see Fig 2B). Our preliminary SAXS data also show that the Protein-A:X complex is ~150Å in diameter (see Fig 2C), thus a q-range of 0.01-0.40Å^{-1} will be appropriate. This will require sample to detector distances of 8m (low-q) and 2m (high-q). Protein is stable at 4ºC, hence we wish to maintain this temperature throughout the experiment. At 5 mg/mL we foresee collecting for 1h (0%), 2h (20%), 4h (40%), 2h (80%) , 1h (100%) at 8m, and half these times at 2m. Thus, for 5 samples and 5 buffers, we will require 30 hours + instrument configuration, empty cell etc. Thus we are asking for 2 days beam time.*

Choice of Instrument

- Clearly demonstrate the need for neutrons and how the instrument is appropriate

  e.g. Because SAXS gives the structure of the entire complex, it is difficult to reach solid conclusions regarding changes in shape of each component in the complex. In order to accurately determine the structure of each component in the complex, we require contrast between the two components, which can be achieved using small-angle neutron contrast variation. Thus, Quokka is the most appropriate instrument to carry out this research.

Data Analysis Overview

- Need to demonstrate that you understand what information your data contains and how you wish to extract this information

  e.g. Data quality will be assessed via linearity of Guinier plots [ref] and estimates of the mass of the scattering particles. We will then use Stuhrmann analysis [ref] to yield basic structural parameters relating to the complex. If data quality is appropriate will use conventional shape restoration programs (such as DAMMIN [ref]), to determine the low resolution structure of the complex and that of Protein A and X. By comparing these low resolution structures to those obtained from SAXS on Protein A and X in isolation, we should be able to determine the nature of any large conformational changes.

Figures

- Figures should complement what is written in the text, and should not be an afterthought
  - Pictorial overview of your system
  - A cartoon of your hypothesis
  - Preliminary data

- These can be incorporated into your PDF (recommended) or attached separately

Summary

- Address all points
- Two pages is not a lot of space to describe your experiment, use the space wisely
- Be aware your scores are weighted (65% towards “Quality of Science” and 35% to “Quality of Planned Experiment”)
- Preliminary data is important
- Seek help from an instrument scientist if inexperienced

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