# Molecular Imaging Lab Interview Problem Set

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Each interviewee is assigned one of the problems below. You need to work it out without assistance, but you are encouraged to cite literatures. The performance in this section will not determine our decision, however, it shows your proficiency and insight in this particular field, and may leave a very good impression.

To ensure fairness, late submissions will not be considered. So please send the answers, however incomplete it might be, BEFORE the deadline. A successful answer is expected to be between one and three A4 papers in length. Both handwritten and printed versions are acceptable. English is encouraged, however, Chinese is also absolutely acceptable.

## 1 In depth

In the author's opinion, there are three obstacles in *in vivo* fluorescence imaging, namely,

- the shallow penetration of the light beams;
- the low quantum yield and concentration of the dye;
- the strong scattering effect of the tissue.

Various strategies have been proposed to solve these problems. Here, you are asked to:

1. Briefly review some of the strategies to increase the imaging depth in *in vivo* fluorescence imaging (corresponding to the first bullet above).
2. Propose a novel strategy to increase the imaging depth, and analyze its feasibility. Here, novelty is more important than feasibility.

## 2 Power of Boron

Boron neutron capture therapy (BNCT) uses the stable isotope $^{10}$B delivered to the lesion to capture thermal/epithermal neutrons generated by a reactor or an accelerator, and kill the targeted cells via nuclear reactions of the capturing process. In clinical applications, positron emission tomography (PET) are often used to guide the BNCT process.

Please answer the following questions:

1. Based on your understanding of BNCT, how can patients benefit from PET monitoring?

2. Design one molecule/material/whatever, or a family of them, that simultaneously enables BNCT and imaging. The imaging here is not limited to PET imaging, and any type of imaging is acceptable. Explain the novelty of this entity. Nota bene: no previously reported entity is allowed as an answer in this section!

# 3 Photothermal in a snap

Traditionally, photothermal therapy in small animal employs a continuous wave (CW) laser as the light source. Is it possible to switch to a pulsed laser?

Please answer the following questions:

1. Very briefly summarize the characteristics of different types of pulsed laser, including their biomedical applications, and their interaction with biological tissues.

2. Present and develop a brief research proposal to explore the application of pulsed laser in photothermal therapy.

# 4 Explore the Explorer

In 2017, there was a paradigm shift in the development of PET scanners, namely, the release of the breakthrough in total-body PET scanners. EXPLORER PET/CT, developed by scientists from UC Davis and several other institutions, has brought the parameters of PET scanners into a different level.

For one thing, if you are not familiar with PET studies, the EXPLORER PET could dramatically shorten the scan time, which was reduced from several minutes, to several seconds.

The problem is, how can physicians and nuclear medicine departments benefit from this machine? Many people are trying to find the 'killer app' of EXPLORER PET but with scarcely any achievements.

In this problem, you are asked to:

1. very briefly summarize the specialty of EXPLORER PET (or total-body PET) scanners relative to conventional PET scanners;

2. propose a specific biomedical application of the EXPLORER PET, which is otherwise impossible with conventional PET scanners.

Nota bene: in the second question, DO NOT repeat what could be found in the literatures, if there is any. We are concerned about the specific biological phenomenon or physiological/pathological conditions. For example, 'imaging the hypoxia microenvironment' is not acceptable as an answer, however, 'early detection of non-Hodgkin's lymphoma' is valid. You need to explain your idea with reasoning and analysis.

These questions below are for archival purpose only, because they have already been used in the previous interviews. Do not answer them!

# A Turn it on

One of the strategies to improve the contrast of *in vivo* fluorescence imaging, is to subtract the original structural image from the fluorescence image. As second near-infrared (NIR-II) window cameras (which utilize InGaAs arrays instead of CCDs) perform badly in terms of weak signal detection, this strategy seems very necessary.

How to design an *in vivo* NIR-II fluorophore, which could be turned on by external stimuli?

Turn on: converted from a no or low emission stat into a highly fluorescent state. External stimuli: including heat/temperature, light radiation, ultrasonic treatment, magnetic field; excluding microenvironment triggering, enzyme cleavage, etc, because they are considered internal. Fluorophore: small molecules or any type of materials are acceptable, even endogeneous substances count.

# B QD rainbow

In multiplexed fluorescence imaging, a serious of fluorophores with different emission peaks are needed, and their emission peaks shall be narrow enough, preferably.

1. Propose a solution to provide a serious of those quantum dots, with the narrow emission peak ranging from 650 nm to 1500 nm, and one product every 50 nm. You can use conventional nanoparticles and assume they are not protected by intellectual properties.

2. Ration on narrowing the emission peak width.

# C Madelung Summation

A Madelung summation, which is customly named, is loosely defined as in Figure 1:

A square array of points is on a two-dimensional plane in the Euclidean measured space, with the 'lattice constant' of 1, and the number of points being $n^2$, $n \in \mathbb{Z}^+$. Poiont x is at the 'center' of the array. The Madelung Summation ($M(n)$) is defined as the summation of the disctances between each point in the $n$th array and the center point x.

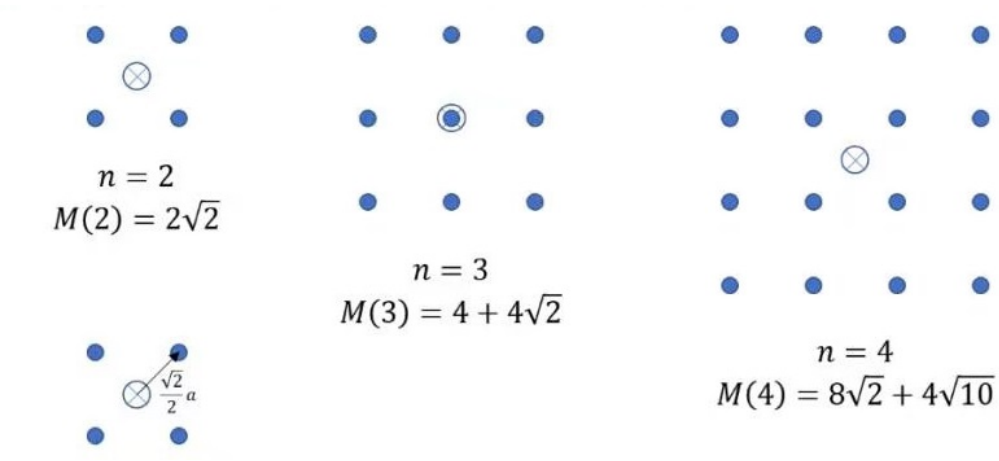


Figure 1: The definition and examples of Madelung summation

It is easy to calculate the first several Madelung summations, as shown in the figure:

$$
\begin{aligned}
M(1) &= 0 \\
M(2) &= 2\sqrt{2} \\
M(3) &= 4 + 4\sqrt{2} \\
M(4) &= 8\sqrt{2} + 4\sqrt{10} \\
&\cdots
\end{aligned}
$$