IMPERIAL COLLEGE LONDON

B.Sc. Examination 2016

This paper is also taken for the relevant examination for the Associateship of the Royal College of Science

SYNTHETIC BIOLOGY

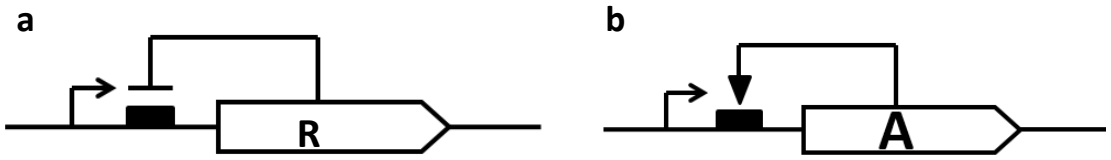
Friday 26 February 2016 10.00 - 13.00

FOR FINAL YEAR STUDENTS IN BIOCHEMISTRY, BIOTECHNOLOGY & BIOLOGY

Answer ONE question from Section A and THREE questions from Section B. Answer each question in a separate book. Parts of a question carry equal weighting unless otherwise specified.

Section A
Answer ONE Question from this section.

1.



a) Explain the topology of the reaction networks shown in **a** and **b** above and define the differential equations for d[R]/dt and d[A]/dt, explaining all terms used. (20%)

b) Explain the dynamics expected of both systems if they are tuned to give equal concentrations of protein at their equilibrium position. (40%)

c) How might these systems be combined to provide a robust oscillating circuit? (40%)

2.

a) A biological waveform is sampled at a sampling frequency f_s and comprises a total of N samples. The waveform is passed through a Fast Fourier Transform in order to obtain its real and imaginary spectra. Draw a fully labelled schematic diagram of both the real and imaginary spectra. A single frequency component has a real value ‘a’ and imaginary value ‘b’. If the amplitude of the waveform at the same frequency is A, what is the relationship between A, a and b? Similarly, if the power in the waveform is P, what is the relationship between P, a and b? (45%)

b) In reality, the waveform is correctly sampled at 0.01Hz and the amplitude spectrum shows that the waveform comprises two components, the first at 0.001Hz and the second at 0.003Hz. Draw the amplitude spectrum of the waveform. Where, for the 0.001Hz component a=1 and b=0.5; and for the 0.003Hz component, a=3 and b=1.5. (15%)

c) As part of the analysis of the waveform, it is decided that filtering should be undertaken in the frequency domain in order to remove the lower frequency component. By means of diagrams similar to those constructed for part (a), explain how this operation would be carried out in the frequency domain. If the time series of the filtered waveform is now required, describe how this can be obtained with a Fast Fourier Transform. (40%)

Section B
Answer THREE Questions from this section.

3. a) The high-level design of a new biosensor is to be carried out in the context of the synthetic biology design cycle. Assuming that only some of the BioParts for the design are available, describe in the form of notes and diagrams the steps which might be undertaken to complete the design. (50%)

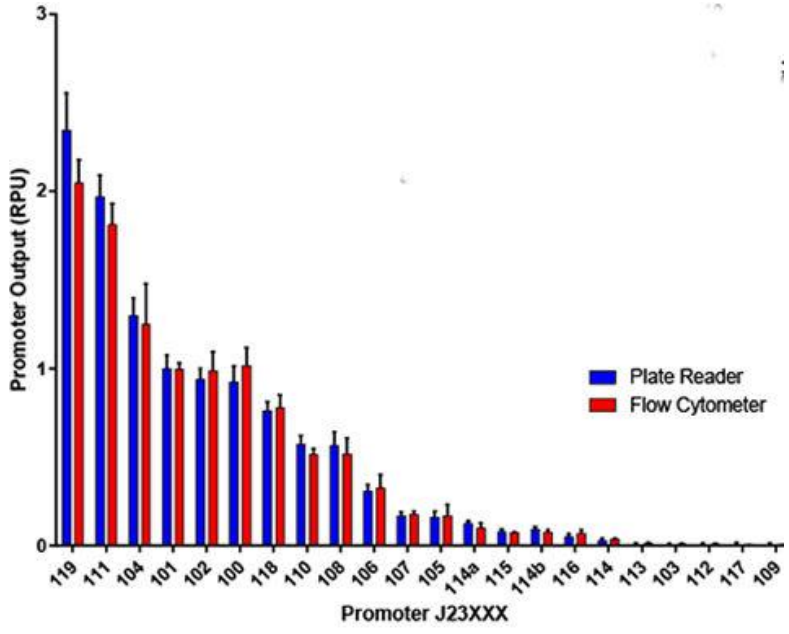
b) Figure 1 shows the outputs of a group of constitutive promoters, where for each promoter the line on the left is the plate reader output and that on the right the flow cytometer output. A single promoter, 101, is being used in the design of a biological AND gate as the promoter for both channels of the AND gate. A simple analysis of the AND gate shows that the dynamic into which the promoter feeds has a frequency response of the form:

$$G(j\omega) = \frac{1}{1 + j\,\omega/a}$$

where a = 0.00088 rad sec^{-1}

The design of the AND gate now needs to change so that it operates 0.0018 rad sec^{-1}. Draw a straight line approximation Bode magnitude plot of the frequency response of the system. Determine the magnitude in response at the new operating frequency and on this basis determine how much the output of the channel promoters need to change to compensate for the change in the dynamic's gain. Using Figure 1, determine which of the promoters might be suitable for this new set of conditions and explain why. (50%)

Figure 1



4. You won the lottery and decided to spend your winnings on making a new synthetic version of the *E. coli* genome to impress the world. The MG1655 K-12 *E. coli* genome is a single 4.64 Million bp circular chromosome, containing approximately 4466 genes.

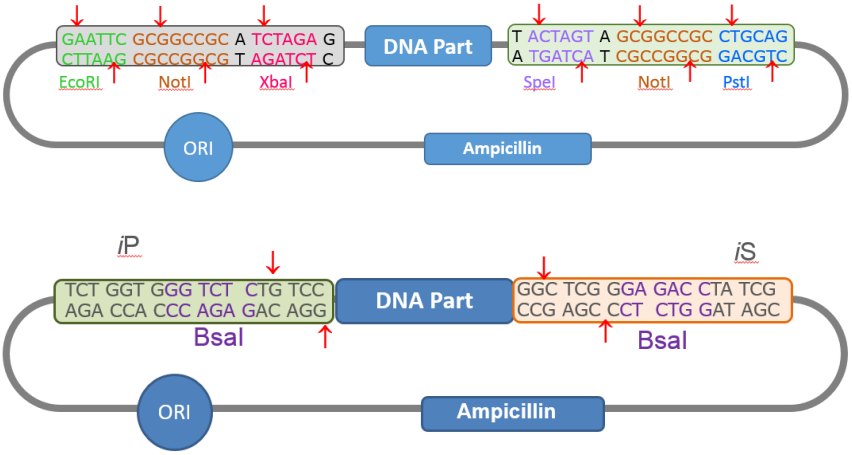
   a) Demonstrating your knowledge of genome synthesis and DNA assembly, how would you construct your new synthetic *E. coli* genome from synthesised DNA pieces? You may use diagrams to aid your answer. (40%)

   b) Describe two design changes you intend to make in your synthetic *E. coli* genome, explaining what the purpose of these changes are and giving details on how these changes can be incorporated into a synthetic genome and how they work in the cell. (40%)

   c) Your lottery win wasn't as big as you thought, so you only have the money to make a 2 Million bp genome containing 2000 genes. How would you choose which genes to include in your reduced *E. coli* genome? (20%)

5. We can say a biological property is 'portable' if we are able to transfer it from one organism to another. Describe and explain the current routine approach to expression of foreign genes in *E. coli*. Explain why this approach works well in some cases, but not others. Discuss how new approaches are addressing current limitations.

6. The standardised formats for both Biobrick and BASIC assembly are shown below. Explain the benefits of standardised DNA assembly formats in synthetic biology and describe the key benefits and limitations when designing and performing assemblies using these two methods.



7. French flag systems represent one of the main theories of biological pattern formation. Using examples, describe how French flag systems function and outline how and why synthetic biologists are aiming to emulate them.

8. From a sociological perspective, “health is more than a medical matter.” What does this mean and what are the implications for implementing a “Responsible Research and Innovation” approach to synthetic biology? Use specific cases to illustrate your answer.

End of paper