The University of Nottingham
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Examination for the degree of PhD - First Submission

Independent Report on the thesis

Each Examiner is required to submit an independent Report on the thesis **in advance of the** *viva voce* examination and to submit it to Student Services or Head of School/Department

School/Dept:	Engineering Faculty
Candidate's name:	Nitzan HERZOG **4199179**
Title of thesis:	Rapid Solution Exchange to Entire Neuronal Cultures Grown on Multi Electrode Arrays
Programme of Study:	**PhD Electrical and Electronic Engineering**
Name of External Examiner:	Dr Mark Wall ✓
Name of Internal Examiner:	Dr Chris Sumner

Please note a copy of this report will be given to the candidate when the examination outcome is notified.

This is a very comprehensive thesis. In the main it is well written and very detailed. It contains some very nice figures with complete legends. The overall aim of the work is to be able to rapidly apply the neuromodulator dopamine to cells which are grown on an MEA with the ability to couple the agonist pulse with the activation of neurons. This is a reduced version of what happens in the brain during reward and reinforcement behaviours.

A lot of the material is methodological and there are only limited results.

In the viva I would like to test the candidates understanding of neurons and electrophysiology. I would like the student to outline what has been achieved in this project. Is it purely a development in experimental methods or have any new results been produced. I would also like to discuss the problems in using neuronal cultures and how this compares to brain tissue.

Date: 18/05/17.

Signature: M. Wall (~~Internal~~/External Examiner*) (*delete as applicable)

Please continue on the second page if necessary and sign each page

SA/22/05/2017

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This thesis is concerned with the development of neuronal cultures on electrode arrays whereby electrical stimulation and recording can be performed whilst pulsing chemicals – principally neurotransmitters – across the surface of the culture. Such a model would allow exploration of the role of neuromodulators in neural plasticity.

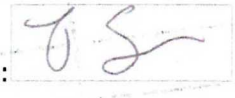
The thesis is for the most part very well written, and displays a good level of scholarliness. I particularly enjoyed the background material, which I was unfamiliar with and so gained personally. I found the structure of the thesis good, with logical progression through the chapters.

There is good evidence of practical endeavour here. It was obvious that this development was long, and seemed to have been performed logically and painstakingly, with incremental benefits as a result.

Finally, the thesis did not really tackle any scientific questions, since the final experiment failed for reasons which are not clear to me. It is also not clear to me what the novel technical developments really are. I would imagine that many of the paths trodden would have been ones trodden before, but that the expertise was presumably not available locally. This will be something worth exploring in the viva, as part of a discussion about what might be publishable.

It is a shame that ultimately Nitzan did not produce any scientific output. I think that the project was heading in an exciting direction. Overall I think the amount of work, clear demonstration of scholarliness and great capability to follow a development goal, and the quality and completeness of the thesis mean that this is well worth a PhD.

Date: 23/5/17.

Signature:  (Internal Examiner*) (*delete as applicable)

Please continue on the second page if necessary and sign each page
SA/03/08/2017

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Examination for the Degree of PhD - First Submission

Joint Report Form

School/Dept:	Engineering Faculty
Candidate's name:	Nitzan HERZOG **4199179**
Title of thesis:	Rapid Solution Exchange to Entire Neuronal Cultures Grown on Multi Electrode Arrays
Programme of Study:	**PhD Electrical and Electronic Engineering**
Name of External Examiner:	Dr Mark Wall
Name of Internal Examiner:	Dr Chris Sumner

A brief report on the thesis examination should be included below.

If the examiners are recommending re-submission for PhD - but have concerns that it may not be possible for the candidate to achieve that standard in the re-submission period, they may inform the candidate that it is advisable to re-submit for MPhil, and if this is done this should be clearly stated here.

If the examiners require the candidate to incorporate revisions contained in their Independent Reports when completing corrections or submitting a thesis for re-examination this should be explicitly stated.

Report on the thesis examination:

Both examiners had independently arrived at very much the same conclusion about the work. The thesis was very well written, logically ordered, comprehensive, and showed evidence of a good amount of work and understanding. Although the PhD might have been very different if so many technical problems had not been met, those challenges were met with rigorous investigation appropriate of doctorate level research.

We agreed that there were a few errors in the thesis, and several points where figures and writing needed to be made clearer.

Date of *viva voce* examination: 25/5/17

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Report on the *viva voce* examination:

Given that the standard of the thesis was good, the main goal of the viva was to check that he knew his material, and wrote the thesis.

Nitzan was able to thoroughly convince us of both these things. He proved himself to be extremely knowledgeable and enthusiastic about his work. In addition he demonstrated a good knowledge basic processes in neuroscience and ability to explain these concepts well: he was tested on his knowledge of action potential generation, neurotransmitters and in particular dopamine (relevant to the thesis).

After a brief discussion we both agreed that there were only a few corrections required and advised Nitzan that he had passed subject to minor corrections.

The principle required corrections are:

Corrections

1) Cut abstract to one side
2) Page 13 line 2 approached
3) Page 18 add a figure to illustrate mea achievements
4) Page 21 add Wall 1997
5) Page 25 line 7 thats STDP
6) Page 28 what about Thomas et al
7) Page 32 poor first sentence
8) Page 33 error line 2 hD work
9) Page 35 figure 2.14 (refered to on line 5) does not exist.
10) Page 51 add scale bar to figure
11) Page 54 add zoomed in photo to show cells
12) Page 55 figure why channel 12 to87
13) Page 57 spelling mistake in figure activity
14) Page 60 line 3 second paragraph "allowed providing"
15) Page 61 figure take A and B labels out of boxes
16) Page 63 add reference to original LTP experiments (Bliss and Lomo) LFP measurements
17) Page 71 figure 3.11 rat cultures vs rat cultures (mouse?)
18) Page 80 remove figure as pointless
19) Page 81 Exapnd figure so it is understandable – add diagrammatic aid as per Dr Sumner's copy of the thesis. Add scale bar to figure.
20) Page 91 figure. Increase size as hard to see what is going on
21) Page 106. Figure 5.5 and the explanation of an offset culture in the semi-permaneable.
22) Page 109 figure??
23) Page 118 tonic inhibitor tonic inhibition?
24) Page 123 we will further showed
25) Correct all instances of units which appear as (for example): $\frac{m}{s}$ to a more standard format such as m/s or ms^{-1}.
26) Throughout the thesis, there are figures showing activity on MEA arrays. The linear displays of activity over time are very confusing as to which row shows which channel. They show only those arrays that are active, but which these are and how it is determined which ones are displayed is not at all clear. We recommend adding an extra panel to the first time this appears, in the methods, to explain this fully.

Candidate's Name: **Nitzan HERZOG** 4199179

27) Check that the vertical axes labelling the channel numbers in the above figures is correct. These might be changed to something clearer?

28) Figure 2.6. these traces do not look like they are high-pass filtered at 200Hz. What exactly are they? Possible correction required to the legend.

29) Figure 3.5. panels C and D have no labels or numbers on the xaxis. Neither do E and F. Please correct any labelling sloppiness throughout the thesis.

30) Figure 6.16. improve figure as suggested.

However, in addition the both examiners provided Nitzan their copies of his thesis, so that he could correct the various typographical errors which the examiners spotted.

SA/03/08/2017

contd..../

Summary of Examiners' Recommendations

Please tick the appropriate box (s)

Award of PhD

☐ without conditions
☐ subject to correction of typographical errors within 1 month[1]
X subject to minor amendments[2] to be completed within 3 months[3]

Referral, with

EITHER

a) resubmission of the thesis within 12 months for PhD:
☐ *viva voce* required
☐ *viva voce* not required

Please Complete this section if 'a)' is selected:
If resubmission for PhD is recommended but the student is unable to re-submit:
☐ MPhil to be awarded now
☐ MPhil to be awarded now subject to minor amendments[2] to be completed within 3 months[3]
☐ Thesis not currently at MPhil level

OR

b) another *viva voce* examination although thesis is accepted
☐ without conditions
☐ subject to minor amendments[2] to be completed within 3 months[3]

Failure at PhD standard

☐ No higher degree to be awarded at all[4]

1 This option should be selected only in instances when the candidate is required to make minor corrections to the text, e.g. typographical errors, which are so minor as to be completed in one month. It is the responsibility of the Internal Examiner to verify that the corrections have been made to his/her satisfaction.

2 Minor amendments are amendments to the thesis not requiring external academic re-assessment, e.g. extensive typographical errors, minor re-organisation of material, addition of supplementary material to clarify the content of the thesis, or removal of extraneous text and may include minor re-writing of material. Minor amendments are in excess of minor corrections but are not, in the opinion of the examiners, sufficient to require the student to be referred and to resubmit. It is the responsibility of the Internal Examiner to verify that amendments have been made to his/her satisfaction.

3 Exceptionally, where a student has been previously registered as a part-time student and it has been demonstrated that circumstances exist such that it would be in the best interests of that student, the examiners may recommend that the degree be awarded subject to minor amendments being completed within six months. Where this option is chosen, please indicate by deleting '3' and replacing with '6'.

4 The University recommends that, other than in exceptional circumstances, Examiners should not normally choose this option on a student's first examination.

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It is confirmed that the *viva voce* examination has been conducted and that the student has been given informal feedback on the outcome of the examination.

Name of External Examiner: **Dr Mark Wall**

Date . . . . . 26/5/2017. . . . . .Signature

Name of Internal Examiner: **Dr Chris Sumner**

Date . . . . . 26/5/2017 . . . . . .Signature

I confirm that the examination process has been completed according to University regulations and procedures[1]. I endorse the Examiners' recommendations.

Signature of Head of School/Dept: Date . . 3 Aug 17 . . .Signature Matt Clark

Matt Clark

PP Donal McNally

[1] For joint/dual awards it is confirmed that the Partner Institution(s) regulations have been satisfied.