

16<sup>th</sup> November 2020

**Review of “Micromanipulation Using Dielectrophoresis: Modeling and Real-Time Optimization-Based Control” by Tomáš Mickálek**

The thesis is very well written, and beautifully presented. Not only are the figures clear, but the use of artistic imagery at the start of each chapter is exquisite. I have never seen this in a thesis, and wish I could see it more often. The standard of English is not only fluent, but highly engaging which makes the thesis very readable. The figures – such as the illustration of DEP on page 4 – is something I would expect to see in a book.

The chapters follow an “assessment by works” model – that is, there is an introduction followed by papers which either have been published, or are scheduled to be published in the near future. Whilst this format demonstrates the quality of the work by dint of it having already been peer reviewed, it does have downsides; not least, it steers the author away from a comprehensive review of the literature. Nevertheless, the candidate gives every appearance of being fully au fait with the background material.

Since the research chapters effectively form discrete items of research, I will consider them separately. The first research chapter presents a study of the effect of higher-order multipoles on the electrokinetic behaviour of particles beyond the dipolar approximation usually considered when analysing dielectrophoresis. The work shows a high degree of rigour in the development of theory, performance of experiments, and in the analysis and discussion of comparing them. This represents some of the most significant work in this area since multipoles in DEP were first explored by TB Jones in the 1980s, though his work is somewhat absent from the citations list (beyond a single review paper).

The remaining three research chapters focus on different aspects of the manipulation of arbitrarily-shaped objects by DEP from a modelling perspective (chapters 3 and 4) validated by an experimental chapter (chapter 5). Considering the first of these, the candidate presents a detailed computational model of DEP behaviour based on the Maxwell Stress Tensor approach. I believe this is very much to be applauded; at present there are sufficient generic finite-element solvers to make it feel like building models from scratch is redundant effort, and this chapter clearly shows this not to be the case. The model is presented in some detail and results are presented, though the results and discussion section is small and no validation of the results is presented, either experimentally or in terms of discussion of prior work in the literature. NB The two authors listed for reference 5 are in fact the same person.

Chapter 4 continues with the computational approach, discussing the potential for using DEP as an assembly tool for microparticles by allowing 3d manipulation through a combination of positioning and electrorotation. This is the chapter I am least convinced by; not because of the quality of the science presented, but because these do not appear to be the best tools to approach the job under discussion; the biggest problem I can foresee is the lack of independent positional control to perform the manoeuvre



shown in figure 4.1; second, for such precise control electro-orientation would be a stronger and more absolute determinant than electrorotation, but hasn't been considered as a design option; third, and most significant, the model excludes Brownian motion, which is one of the most significant forces at this scale. The electrokinetic model looks robust; the hydrodynamic model is good but conventional (it doesn't include electrohydrodynamic effects, for example). The experimental section is comprehensive but doesn't include the number of technical repeats in order to assess dependence on factors such as initial position. The work on eccentricity is good but work like this has been done before (MP Hughes, Phys. Med. Biol. 1998 12 3639-3648). The experimental section is of good quality. However, the key point of this part of the work is the comparison between theory and experiment on page 92, which is exemplary; the quality of fit is excellent and the discussion is convincing.

Chapter 5 continues in the same vein; it describes a control system to manipulate the position and orientation of a complex-shaped particle. The rationale of the system for positioning complex objects is again slightly superfluous, not least because as before it doesn't address some of the complexities of manipulating multiple objects – and also misses easier applications to which this system could be eminently suited, such as positioning sperm with respect to egg. But as before, when we look past these more complex aims and just look at the science as presented, the work is again of very high quality, with an excellent theoretical/experimental study of combined DEP and electrorotation. As before, I would have liked to see the early studies represented in the literature (e.g. Y Huang et al 1992 Phys. Med. Biol. 37 1499), but the work presented here certainly moves the field along substantially.

The conclusion presents not only a useful summary, but a discussion of the potential for applications for the platform outlined in the thesis. There are some oversights regarding potential drawbacks of the technology for manipulation of multiple micro-objects, not least the potential problems with needing to move objects in different directions and the requirement for objects to be manipulated to be kept within the inter-electrode space. The review of computational limitations is also good.

In summary, the thesis represents a clearly novel body of work in which a problem – that of manipulating arbitrarily-shaped objects by dielectrophoresis – has been approached from multiple angles. There are occasional distractions in the form of discussions about complex plans for fabrication, but shorn of this the thesis represents a comprehensive study of numerical, analytical and experimental approaches to the dielectrophoresis of arbitrarily shaped objects, in which the degree of consistency between model and experimental result is excellent. I strongly believe that this scientific underpinning will be of great importance to the future of the field; people will refer back to the work (and its published components) for many years due to the comprehensive way in which it has advanced the theory in the area. The objectives – that of building a comprehensive and validatable model of the electrostatic electromanipulation of arbitrarily-shaped particles – have clearly been met.

The work is clearly novel, rigorous and inventive, and on the basis of this I believe it shows clear evidence that the standard of work is appropriate for the award of a PhD; the author of the thesis has proved to have an ability to perform research and to achieve scientific results. I recommend the thesis for presentation with the aim of receiving a Ph.D. degree.

Yours sincerely,

Professor Michael P. Hughes

