MICROFLUIDIC REACTION OPTMISATION USING INTELLIGENT FEEDBACK.

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ABSTRACT

A system for the automated optimisation of chemical reactions within microfluidic devices using intelligent feedback is described. Various search algorithms are employed and their utility and performance compared.

Keywords: Synthesis, optimisation, control systems, feedback.

1. INTRODUCTION

Microfluidic synthesis offers many advantages over conventional bulk synthesis; reactions can be performed in a continuous flow configuration, allowing facile online monitoring and high-throughput reaction screening to be performed[1]. These features mean that reaction optimisation can be performed with a tiny fraction of the time, expense and effort usually required. Since reaction optimisation can save a company many millions of pounds[2] in the form of higher yields and fewer byproducts, this capability is of great commercial interest.

The focus of this work is the creation of an entirely automated system for optimising a continuous-flow microfluidic synthesis. The system must be suitable for a wide variety of different reactions, and must be able to find a suitable optimum rapidly and with no other user input.

2. THEORY

A number of algorithms were investigated in order to determine which were best able to cope with real-world synthetic conditions. These algorithms can all be considered to be topological operations on a multidimensional "configuration space" where the axes of this configuration space correspond to the flow rates of the pumps. They are as follows:

Simplex Algorithm – A series of test points are created in configuration space, and a new point to test is created by moving away from the worst point.

Nelder Mead Simplex Algorithm – As above, but the simplex is permitted to change shape to better fit the contours of configuration space.

Pattern Search – a starting point is found and a series of test points are generated in the area most likely to produce a better result. The next starting point is generated by drawing a line from the start point, through the best test point to a final point beyond.

Look / Monte Carlo – points are tested at random in the vicinity of the current 'best' point, and if a better point is found, points are generated around that instead.

Genetic Algorithm – Each flow rate is considered as a gene on an artificial genome, and the configurations producing the best yield are "mated" in order to produce offspring with similar characteristics in the next generation.

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3. EXPERIMENTAL

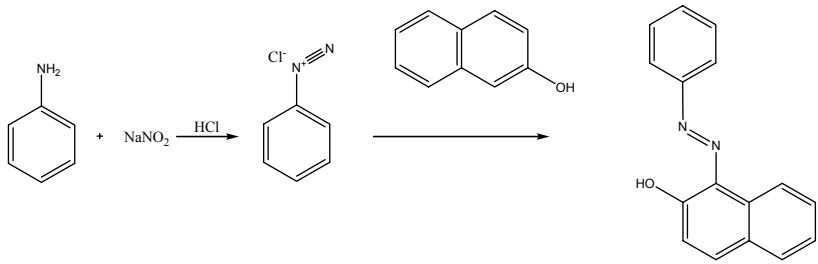
Automated Microfluidic Synthesis System

The microfluidic synthesis system consisted of a series of computer-controlled syringe pumps which controlled the flow of reagents into a glass microfluidic reactor. Optical fibers were placed on either side of the exit channel of the reactor. One fiber was coupled to an Ocean Optics HL-2000 tungsten halogen light source (7W output) and the other was coupled into an Ocean Optics USB2000 Vis-NIR spectrometer.

The spectrometer was connected to the same computer as the pumps, and the entire experiment was controlled using a custom-built control program written using Labview 7.1 from National Instruments. The spectrum was analysed by the computer in order to determine the concentration of product by using the Beer-Lambert Law, and the resulting yield was used to determine the next setting to be used by the pumps.

Experimental Results

The reaction that was selected for optimisation was a two-step synthesis of Sudan I:



Scheme 1. Synthesis of Sudan 1

A series of different algorithms were tested in order to determine the speed of convergence and the quality of the optimum. The results are shown below; the vertical axis

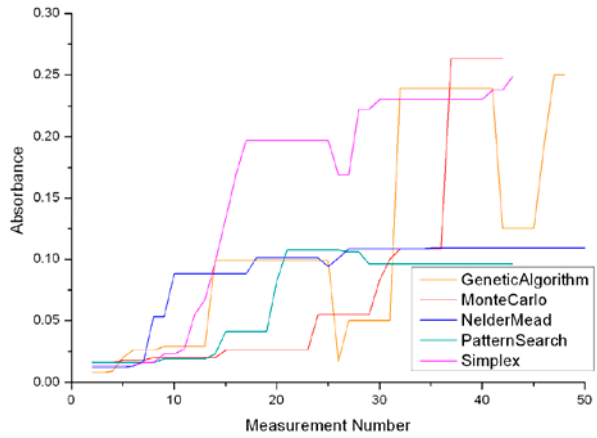


Figure 1. Results of optimisation of Sudan synthesis by various algorithms

measures the highest absorbance measured up until that point by the algorithm and is a direct measure of the concentration of Sudan I produced by those reaction conditions. Downward steps are caused when the reaction conditions are re-evaluated and found to be lower. This function serves to reduce the effect of experimental noise on the measured optimum.

RESULTS AND DISCUSSION

The results of this optimisation were typical of other optimisation runs performed on this synthesis and also reflected the relative performance characteristics on other chemical syntheses. Some common observations on the algorithms are outlined below:

Simplex Algorithm – generally this performed well and was resilient towards experimental fluctuations. Since a major cause of error in the experiment was the system having insufficient time to settle down if the reaction conditions were varied a great deal, the fact that the simplex algorithm only makes incremental changes to the reaction conditions meant that it rarely had to re-evaluate a peak. Convergence time was generally acceptable, and the optima were good.

Look / Monte Carlo – this performed reasonably well over time but its tendency to rapidly change reaction conditions lead to costly errors. Performance fluctuated a great deal, as can be expected.

Genetic Algorithm – this generally outperformed the Look algorithm but suffered from the same tendency to vary the reaction conditions rapidly. Performance was better on more higher-dimensional problems; on simple syntheses with only one or two variables it was often outperformed and no better than the Look Algorithm.

Nelder Mead Simplex Algorithm – performance was good when there was little experimental error, however since the simplex will shrink in certain conditions, occasionally it shrinks for no reason, costing the algorithm a great deal of time, making it's progression slower and consequently lowering the quality of the optimum.

Pattern Search – similar problems affected the pattern search, however, it expands more readily so in general managed to cope better than the Nelder Mead Simplex.

CONCLUSION

This work represents the beginning of a completely automatic system for the optimisation of a chemical reaction, with the potential to revolutionise bulk synthesis of industrial chemicals. A series of different optimisation algorithms have been evaluated and their performances analysed.

Generally the Simplex Algorithm performed the best, finding a good optimum quite rapidly, with good tolerance for random fluctuations and reliably moving towards the theoretical optimum.

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