

Autonomous Experimentation: Coupling Active Learning with Computer Controlled Microfluidics

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The interactions of biomolecular substrates, such as networks of enzymes, exhibit behaviours that could allow for new modes of information processing [1]. Information processing is not required to work within physiological conditions, therefore the contribution of existing knowledge about enzyme interactions is limited. New knowledge about the interactions of enzymes can only be obtained experimentally. However, the high dimensionality of the parameter spaces mean that the resources available are limited compared to the size of the space to explore. Often this can leave at most a handful of experiments per parameter dimension. Additionally, the validity of experimentally obtained observations are not guaranteed, particularly in the biological domain where experimental error can produce observations not representative of the true behaviour. By combining active learning techniques with an automated lab-on-chip platform, we are working towards a fully autonomous machine. This machine will provide effective resource usage, achieved through both minimising the number of experiments required to be performed and by reducing the chemical resources consumed in each experiment.

Autonomous experimentation, as shown in figure 1, is a closed-loop technique consisting of three main components. The hypothesis manager proposes and maintains a set of possible models for the observations obtained. The experiment manager uses information from the hypotheses and previous experiments to determine the next experiment to perform. The parameters of these experiments are passed automatically to an automated experimentation platform, in this case a lab-on-chip device, that physically performs the experiment and returns the observations to the computational system.

Our prototype algorithms have been shown to work effectively in limited resource scenarios where the validity of observations are not guaranteed. We address the problem of erroneous observations by utilising a multiple hypotheses approach, where potentially erroneous observations are considered as valid and erroneous by competing hypotheses in parallel. Decisions about the validity of those observations are then postponed until further experimental evidence is available.

Currently we are considering methods for actively selecting experiments to efficiently differentiate between competing hypotheses. Additionally, in parallel a fully automated lab-on-chip device is in development with capabilities such as mixing and optical absorbance analysis to be performed on-chip. In the near future we look to combine the algorithms developed with the automated hardware to create a fully autonomous experimentation machine capable of effective analysis of the interactions of biomolecular substrates.

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References

- [1] Zauner, K.-P. & Conrad, M. Enzymatic computing. *Biotechnol. Prog.* **17**, 553–559 (2001).

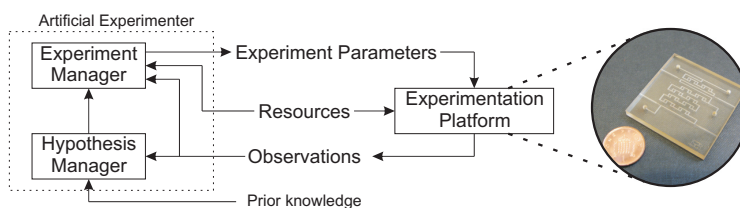


Figure 1: Cycle of experimentation in an autonomous experimentation machine.