PIPETMAX® and Antha
Rapid, Robust, Single-Well DNA Assembly

TECHNICAL NOTE TN219

For researchers in biopharmaceutical R&D, the accurate and rapid assembly of genetic constructs is a crucial aspect of their work. Existing methods using manual and conventional cloning techniques are time-consuming, require expensive temperature control equipment, and entail multiple error-prone preparative steps, e.g., gel extraction or restriction digestion. Their manual implementation requires extensive liquid handling, often leading to the mislabelling of samples or the use of the wrong reagent, contributing to high levels of irreproducibility within the biological scientific literature.

Antha Type IIS Assembly

The Antha Type IIS method assembles DNA parts directly from clonal vectors in a one-pot reaction, at room temperature. This makes it ideal for fully automated execution on simple liquid handling robots, without the need for temperature control or thermo-cycling. DNA parts require no special preparation such as pre-digestion, gel purification or PCR: dramatically increasing efficiency, fidelity and robustness. The method generates dozens of assemblies per liquid handling robot in a few hours.

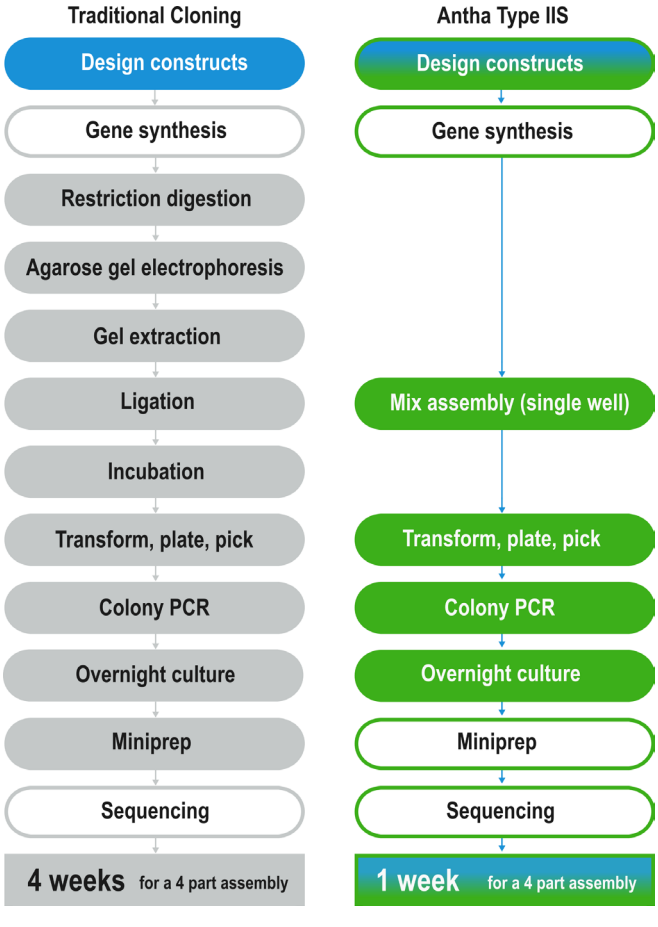

Figure 1
Synthace's TypeIIS assembly method is significantly streamlined versus a traditional Golden Gate Assembly method.

SYNTHACE | GILSON®

In contrast to other protocols, such as the Golden Gate Assembly and Gibson Assembly®, the Antha Type IIS Construct Assembly is the only workflow that combines the power of digital automation with biological operational simplicity, all whilst not sacrificing the complexity of constructs that can be generated. Central to this is the biological operating system developed by Synthace – Antha.[1] Antha defines exactly what needs to happen to all the input DNA parts in order for them to be assembled into the final constructs designed by the biologist and directly instructs liquid handling robots to carry out the assembly. This ensures that the DNA assembly is run exactly to the optimized robust protocol and frees the biologist to think about what constructs they want to test, and not about how to make them. In addition, due to the exceptionally flexible nature of the Antha language, the construct assembly protocol can be rapidly linked with other elements, e.g., transformation and plate-out, to create sophisticated biological experimentation workflows.

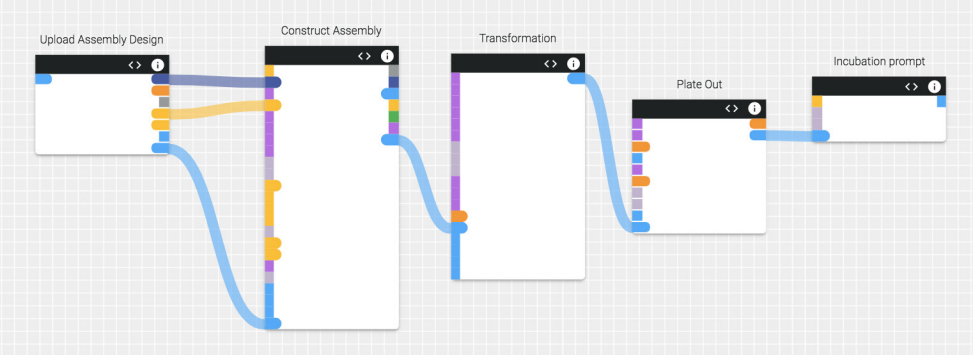

Figure 2
Antha's drag and drop interface enables fast set up of flexible methods, including import of DNA assembly designs and export of ready-to-run PIPETMAX® methods.

Case Study - Automated Antibody Assembly

Synthace's client, a leading multinational pharmaceutical company, sought to optimize their combinatorial antibody construct assembly and thus looked to deploy Antha into their existing workflow. Multiple heavy and light chain constructs were assembled combinatorially, utilizing four or three components in each reaction using Antha controlled automation, an assembly success rate of 97% was achieved. To undertake this workflow, the design file was simply dragged and dropped into Antha. Antha seamlessly validates the assembly in-silico using a proprietary active learning algorithm, the software then detailed the plate layout necessary for the user to set-up the experiment (Figure 4, far right). The Gilson PIPETMAX subsequently undertook the liquid handling steps under the control of Antha saving hours of laborious and error-prone manual pipetting. As the process is automated and controlled through software, reproducing experiments is made easy for the user – as is tracking sample provenance during experiments, an important benefit in complex DOE methods or biologics workflows.

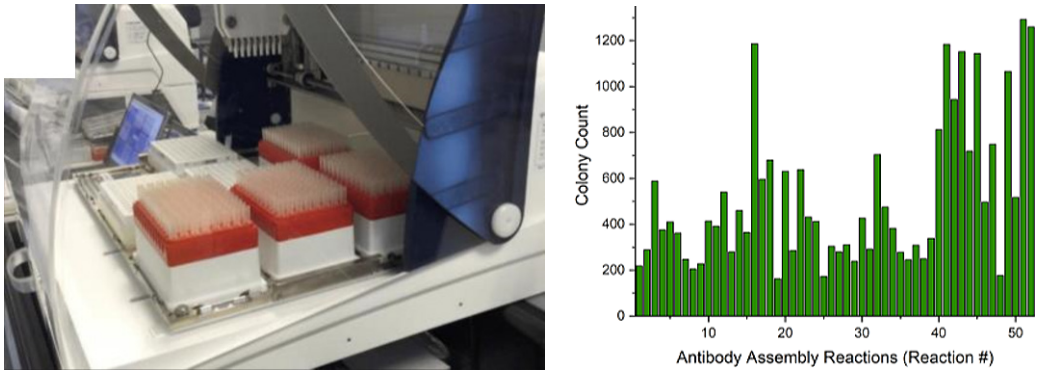

Figure 3
(left) Using Antha, the Gilson PIPETMAX® was rapidly set-up before the subsequent assembly experiment was run through the Antha software platform. (right) All reactions produced colonies, 97% of which contained the clonally correct construct.

The example given here illustrates a simple proof of concept case for easily integrating Antha into your existing laboratory. With support for automated liquid handlers, including the Gilson PIPETMAX, Antha can integrate into your laboratory easily. Furthermore, with applications rapidly coming on-line for advanced bioprocessing solutions, integrated data analysis, assay development, and drivers for more pieces of lab hardware the opportunities for transforming your lab's productivity are endless.

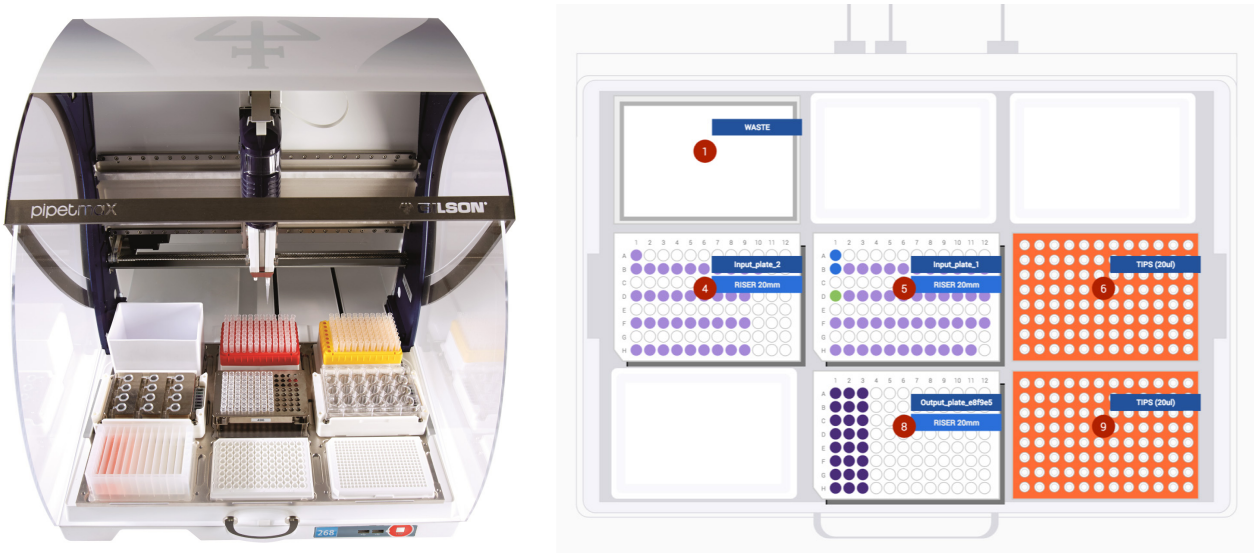

Figure 4
Antha users can configure and export ready-to-run protocols for PIPETMAX® (left), a fully automated personal pipetting station built around PIPETMAN® technology, and can view setup information (right) from within the software.

References

[1] Sadowski, Michael I. *et al.*, Trends in Biotechnology , Volume 34 , Issue 3 , 214 - 227