White Paper

Accelerating Timelines in Digital Biology: The Gibson SOLA Platform

Abstract

In the rapidly evolving field of digital biology, the demand for swift and efficient synthesis of DNA and mRNA has exceeded capacity at service providers. Geopolitical uncertainty and the risk of another global health crisis further underscores the need to gain control over availability of dsDNA, oligos, mRNA, and RNA components. Traditional reliance on external service providers often results in extended timelines, hindering research, development, and scalable DNA-based solutions such as diagnostic tests. The Gibson SOLA® Platform by Telesis Bio offers an innovative solution, enabling laboratories to autonomously generate high-fidelity DNA and mRNA overnight. This white paper explores how the Gibson SOLA Platform accelerates timelines in digital biology, enhancing productivity and providing researchers with greater control over their workflows.

Introduction

The landscape of biological research is increasingly driven by the need for rapid synthesis of genetic materials. Traditional methods, which often involve outsourcing to service providers, can lead to delays spanning weeks to months, from the initial request for a quote to the receipt of constructs. Delays in receiving DNA and RNA constructs are becoming longer due to the increased utilization of Minimal Resistance Disease (MRD) and other applications. These delays impede the pace of innovation and discovery. The Gibson SOLA Platform addresses these challenges by offering an in-lab solution that significantly reduces synthesis time.

Challenges with traditional DNA and mRNA synthesis

Outsourcing DNA and mRNA synthesis presents several challenges

Extended Timelines: Receiving DNA from service providers presents several challenges that significantly impact research efficiency. One of the most pressing issues is extended timelines, where the process from requesting a quote to obtaining the final product can take up to six weeks or longer. This delay is often caused by bottlenecks in synthesis capacity, quality control procedures, and shipping logistics. Additionally, providers may experience supply chain disruptions, such as shortages of critical reagents or unexpected regulatory compliance requirements, further pushing back delivery dates. Moreover, some DNA service providers impose batch processing policies, meaning smaller orders must wait until enough requests accumulate before production begins, extending lead times unpredictably. Customization constraints also play a role - while many providers offer standardized synthesis, specialized requests for long or complex sequences, specific modifications, or high-purity requirements can extend production timelines further. These challenges collectively slow down research progress, forcing scientists to plan months ahead and consider alternative strategies to mitigate delays in obtaining crucial DNA sequences.

Limited Control: One of the major challenges in obtaining DNA from service providers is the limited control over synthesis process and timelines. Since external providers handle every step - from order processing to synthesis, quality control, and shipping - scientists often lack visibility into production stages, making it difficult to anticipate or mitigate delays. Many DNA synthesis companies do not provide real-time tracking or status updates, leaving scientists uncertain about their order's progress. This lack of transparency can be particularly problematic when working with tight deadlines, as unexpected production bottlenecks or quality control failures may only be communicated after significant delays. Additionally, providers often prioritize bulk orders or larger clients, pushing smaller custom orders further down the queue. When issues arise - such

as errors in sequence synthesis, reagent shortages, or regulatory compliance checks - researchers have little recourse but to wait, often with limited options to expedite their orders. Furthermore, customization requests, such as modifications or specific purity levels, can extend processing times unpredictably. Without direct oversight or influence over these factors, research projects dependent on synthesized DNA must be planned cautiously, factoring in delays that are often outside the control of the requesting lab.

Inflexibility: One of the significant challenges of obtaining DNA from service providers is inflexibility, particularly when project scopes need adjustments or iterative changes arise. Unlike in-house synthesis, where modifications can be made in real time, working with third-party providers often means adhering to rigid processes that do not accommodate mid-course corrections. Once an order is placed, even minor sequence modifications or adjustments to synthesis parameters can require canceling and reordering, leading to additional costs and extended timelines. Many providers operate with automated pipelines that prioritize efficiency over customization, making it difficult to implement last-minute changes without disrupting production workflows. Furthermore, standard turnaround times do not account for iterative experimentation, where researchers may need to refine sequences based on preliminary results. This lack of flexibility can slow innovation, particularly in fast-paced fields such as synthetic biology and genetic engineering.

The Gibson SOLA Platform: A paradigm shift

The Gibson SOLA Platform modernizes the synthesis process by enabling on-site, automated production of DNA and mRNA. Key features include:

- **Rapid synthesis:** Traditional DNA synthesis workflows can take 2 to 6 weeks for external providers to generate sequence-verified plasmids, delaying research progress. The Gibson SOLA Platform revolutionizes this process by enabling high-speed, in-house DNA assembly, reducing synthesis time from weeks to just one day. By integrating design and build steps into an automated workflow, SOLA produces sequence-confirmed plasmid DNA (pDNA) rapidly, allowing researchers to move directly to transfection and candidate identification within a week.

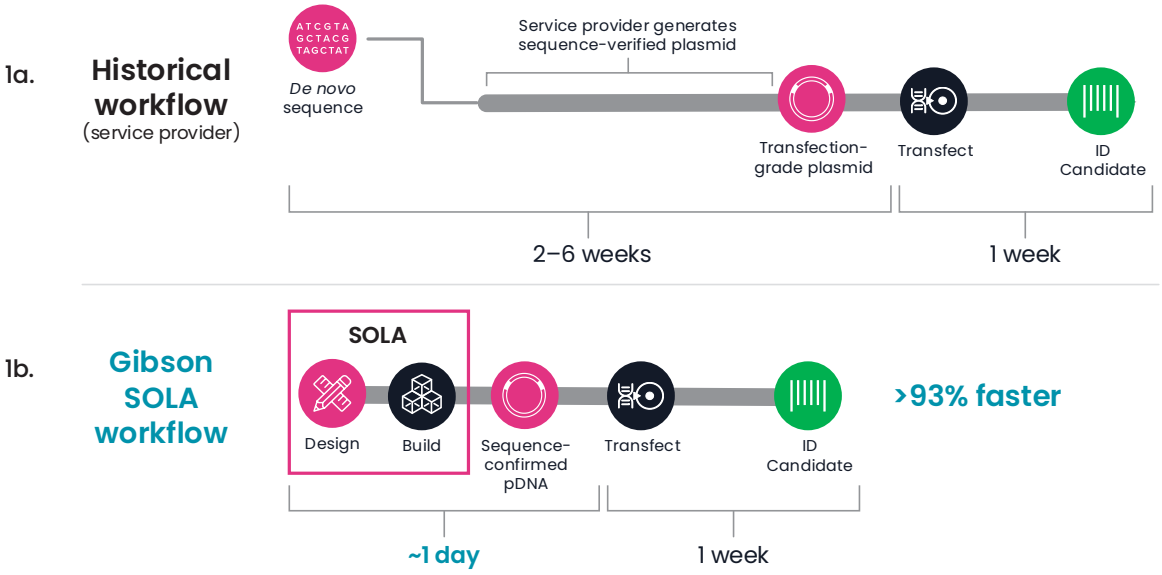

Figure 1. Complete projects more quickly. Eliminate bottlenecks and reduce dependence on external providers by building biology overnight. Historically, service providers can require up to 6 weeks to prepare transfection-grade plasmids (1a). The Gibson SOLA Platform generates pDNA in 1 day (1b).

- **Enhanced control:** On-site synthesis provides full visibility into the process, allowing for better planning and execution. Digital tools evaluate sequences and transparently suggest optional changes when relevant. System logs provide insight into the status of each step and can be monitored remotely.
- **Scalability:** The platform can scale from 20 kb per week to hundreds of kb per day. A single workflow scales from discovery to production with ease. It is no longer necessary to have long delays for contracts, updated specifications, or negotiations to obtain production-grade DNA and mRNA.

Technological advancements boost efficiency

Block-Based Assembly: Gibson SOLA is a powerful molecular biology technique that addresses many of the challenges associated with traditional enzymatic DNA synthesis approaches, such as TdT synthesis. By using a block-based assembly approach rather than single-base addition, Gibson SOLA significantly improves sequence fidelity and flexibility issues faced by other enzymatic methods. By leveraging pre-assembled, qualified short building blocks, it achieves high-fidelity synthesis without the sequence bias or homopolymer issues seen in conventional enzymatic approaches.

The method involves a cyclical process of digestion and ligation to assemble short building blocks into larger sequences. This is followed by a short round of PCR to enrich for correctly assembled sequences, improving the overall fidelity of the final product. The Gibson SOLA process requires significantly fewer steps as compared to traditional synthesis methods, eliminating much of the potential for introducing errors faced by other synthesis methods.

The higher fidelity of the Gibson SOLA Platform also lends itself to improved flexibility by leveraging the block-based assembly process. By introducing conserved sequences of DNA with appropriate sequence overhangs, these external "blocks" can be seamlessly incorporated into the Gibson SOLA Platform, improving the range of sequences that can be synthesized. In addition, while the Gibson SOLA Platform natively yields upwards of 1 µg, due to the assembly process, this yield can be scaled to meet higher experimental input requirements without additional PCR cycles.

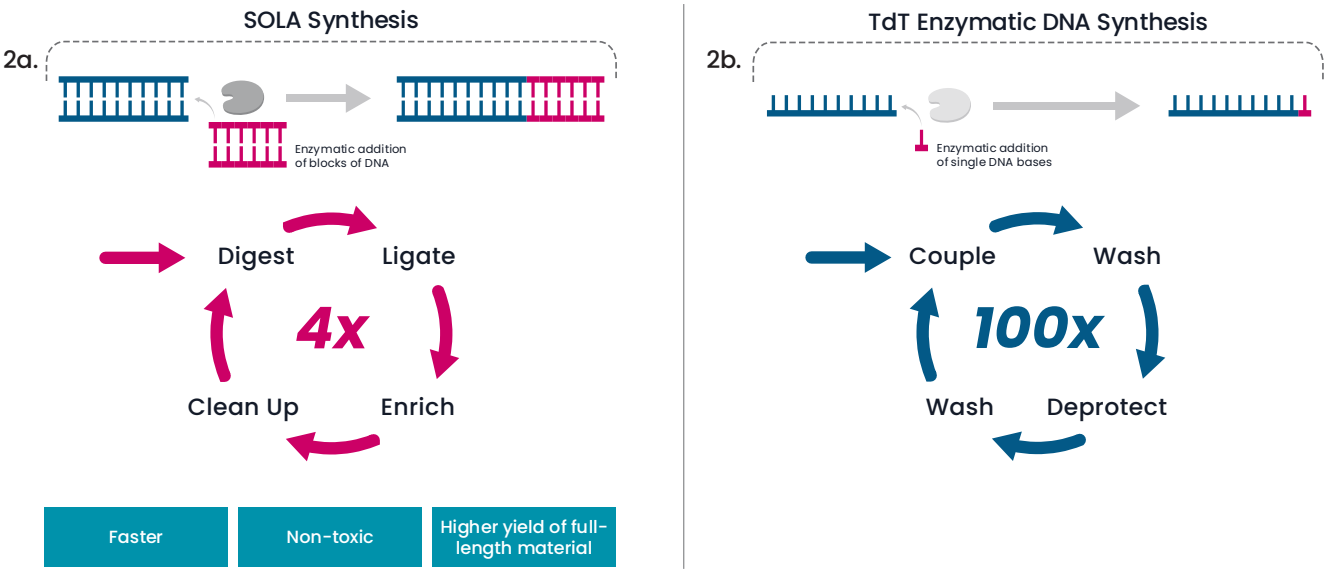

Figure 2a. By starting with pre-qualified, short building blocks, the Gibson SOLA Platform enables the on-demand synthesis of 100bp DNA constructs with significantly fewer steps than traditional DNA synthesis methods. This results in faster completion times compared to outsourcing to service providers while leveraging non-toxic reagents to achieve a higher yield of the desired full-length product.

Figure 2b. Historical approaches to DNA synthesis build DNA strands one base at a time, introducing complexity and errors with each base. The accumulation of mis-bases leads to a reduction in usable yield and restricts buildable sequences.

High Fidelity: A key factor in the success of this technique is the high-fidelity synthesis of DNA fragments, which directly impacts the efficiency, accuracy, and yield of full-length sequences.

High-fidelity synthesis ensures that the DNA fragments generated by the Gibson SOLA Platform are free from errors such as mutations, truncations, or premature terminations. These errors can significantly affect the ability of fragments to anneal correctly, leading to incomplete or misassembled constructs. By optimizing synthesis conditions and using high-fidelity polymerases, the likelihood of producing full-length, functional sequences increases, reducing the need for multiple rounds of re-synthesis and troubleshooting.

This approach also enhances the efficiency of the Gibson SOLA Platform by ensuring that DNA fragments have the correct overlapping regions required for precise annealing. With minimal sequence errors, exonuclease processing and polymerase gap-filling occur smoothly, resulting in higher assembly success rates (Figure 3).

By prioritizing high-fidelity synthesis, scientists can streamline their workflows, improve experimental reliability, and minimize time lost due to sequence errors or failed assemblies.

	Average error rate = 1 per ~180,000 bp Median error rate = 1 per ~90,000 bp			Error-FreeDNA
	Total Reads	Error-Free Reads	Length (bp)	
TBIO_105	9,236	9,005	2,842	97.4%
TBIO_205	9,498	9,030	2,079	95.1%
TBIO_305	8,736	7,921	1,858	90.7%
TBIO_405	8,849	8,487	3,555	95.9%
TBIO_505	9,073	8,721	3,475	96.1%
TBIO_605	9,481	8,619	3,494	90.1%
TBIO_705	9,422	9,279	3,522	98.4%
TBIO_805	9,059	8,945	6,336	98.7%
TBIO_905	9,902	9,756	7,337	98.5%

PacBio® HiFi average depth /position/amplicon = ~10,000X
Following PacBio Amplicon Analysis (https://github.com/PacificBiosciences/pbAA)

Figure 3. Generate high fidelity DNA. Representative data showing nine amplicons sequenced on a PacBio HiFi NGS system at an average depth of 10,000x per position. Error-free amplicons ranging in size from 1.8 to 6.3 kb were generated with an average error rate of 1 per 180,000 bp and a median error rate of 1 per 90,000 bp.

Impact on Research and Development

By integrating the Gibson SOLA Platform into their workflows, laboratories can:

- **Accelerate data generation:** Transition from monthly to daily data sets, expediting the research cycle.
- **Enhance productivity:** Reduce bottlenecks associated with external synthesis services, allowing for more experiments in less time.
- **Increase flexibility:** Easily make iterative changes to projects without the constraints imposed by third-party providers.

Conclusion

The Gibson SOLA Platform represents a significant advancement in digital biology, offering a solution that accelerates timelines, enhances control, and increases productivity in DNA and mRNA synthesis. By adopting this platform, laboratories can overcome the limitations of traditional synthesis methods and drive innovation more quickly.

Find out how automated DNA or mRNA synthesis can accelerate your workflow. Visit telesisbio.com/sola