TeselaGen Biotechnology

Revolutionizing Biological Systems Design

TeselaGen™ is a revolutionary DNA design and assembly protocol generation service providing the most advanced Bio CAD/CAM system available. Recent advances beyond traditional cloning have opened new opportunities in all aspects of biotechnology. These advances are being made in response to the increasing demand for complex DNA assemblies, up to and including entire genomes and/or large combinatorial libraries. With TeselaGen's proprietary technology, these advances are now available for biologists at all levels who wish to assemble DNA simply, reliably, inexpensively, and with high fidelity.

DNA assembly allows biologists to engineer cells to more efficiently and inexpensively carry out desirable operations, such as producing a wide range of molecules for industrial or medicinal use or enabling chemical processes to proceed using biological mechanisms. Biologists pursuing these goals regularly seek to combine genes encoding a series of enzymes that perform the necessary reactions. This requires splicing together DNA parts – genes for multiple enzymes and shorter DNA sequences that regulate expression of those genes – to form recombinant DNA assemblies. The DNA assemblies are transformed into host cells, where they are expressed to produce the enzymes that carry out targeted reactions. While many of the steps involved in this type of genetic engineering have become easier with technological advances in the past several decades, the design of complex DNA assemblies and efficient testing for function have been and continue to be very difficult and time consuming. Indeed the situation is getting more difficult, not less, as assemblies of increasing complexity and variability are becoming more and more important for research and development in areas such as disease treatment, renewable energy, environmental remediation, and agriculture.

By taking advantage of a range of modern cloning techniques as well as outside synthesis services, TeselaGen overcomes the limitations of traditional cloning allowing for the development of scar-less DNA in a more time and cost efficient way. Traditional cloning only offers the capability to put together two pieces of DNA at a time. In its time, that was an adequate solution. Today, making many different constructs, with many pieces of DNA or putting together multiple pieces of DNA into the same construct is a requirement that exposes traditional cloning's fundamental restrictions. TeselaGen supports a broad range of modern assembly techniques as well as outside synthesis services and decouples DNA design from any underlying assembly paradigm. Taking this approach releases the biologist from the major time, cost, and functionality limitations of traditional cloning to not only deliver the best overall assembly protocol, but to also create DNA constructs unachievable by any other means.

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Time Efficiency and Scalability

Using modern standardized techniques employing the exact same reagents at every step, TeselaGen allows many pieces of DNA to be assembled at the same time in the same reaction. Assembly steps can be chained without limit.

Traditional cloning methodologies are highly serialized and ad hoc, where each design step is highly context dependent on the specific molecule being built. Every time one adds a piece of DNA into a vector, an available and unique restriction site must be identified and restriction site-specific reagents used. Once a restriction site has been used, it cannot be reused in a subsequent reaction. For multiple steps, there is no standard methodology and each addition is highly specific to what happened earlier and what needs to happen next. As a result, traditional methods require significant upfront planning time to determine the exact restriction sites and reagents to be used for each step. Given a list of available restriction sites, while the first step in an effort may be relatively easy to perform, subsequent additions are presented with fewer and fewer choices as the available restriction sites are depleted. At some point, all the available restriction sites are exhausted making it impossible to make further additions.

Assuming you have all the reagents and the designs in place, a traditional cloning step usually takes about a week. Adding ten pieces of DNA, if you could do it, would take ten weeks. By using more modern methodologies, TeselaGen removes restriction site constraints from DNA assembly and uses the exact same reagents in every assembly step. With TeselaGen, one could complete the entire ten-step process in one-step and one week.

Trying to scale with robotic automation further amplifies the limitations of traditional cloning. Conventionally, the sequence you wish to construct is constrained by the available restriction sites and enzymes. Thus, on a robotic platform, one would potentially need to use different reagents in every well. With each step different from the rest, the process of adding multiple DNA segments becomes an ad hoc, non-standard process that scales very poorly.

TeselaGen's modern techniques are sequence independent and its design processes and algorithms are completely independent of the DNA being developed. With TeselaGen, irrespective of whether the DNA is being built for green, red or white biotech applications, the assembly protocol is developed in the exact same way. Because these methods are standardized, TeselaGen is extremely scalable, allowing the biologist to pursue unrelated DNA construction projects together in parallel on the same robotic platform at the same time.

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Optimization

One of the most powerful features of TeselaGen is its ability to cost optimize DNA assembly. The principle decision in developing new DNA is often whether to produce it "in house", contract with an outside DNA synthesis service company, or some combination of both. In house production requires a choice between traditional cloning and the newer more modern methodologies embodied by TeselaGen. Outside service providers each have their own pricing and scheduling for fulfillment. Decoupling DNA design from its assembly gives a biologist maximum flexibility in achieving project goals in a cost efficient manner.

Taking the outsourced DNA synthesis route usually implies the direct synthesis of new DNA a single base pair at a time. Direct synthesis can be used to create optimized sub-assemblies that can then be assembled into longer continuous constructs. With TeselaGen, the option of direct synthesis is preserved while allowing for the cost effective option of including already available DNA fragments from existing inventory. Because TeselaGen fully leverages all available synthesis routes, it can optimize the assembly method to achieve the lowest possible cost. Services like IDT, Genscript, or DNA2.0 can easily be leveraged by TeselaGen when it is cost effective to do so. Because TeselaGen has access to all available synthesis routes, it will typically produce a much more cost effective solution than any specific DNA synthesis option.

TeselaGen allows for the incremental accumulation and application of design rules as new biological knowledge is acquired. When building DNA libraries, it is well understood that certain combinations of parts will not yield functional constructs. Design rules allow for the automatic elimination of constructs that are known dead ends. As one automates and scales up to combinatorial libraries with millions of constructs, this type of automated assessment becomes essential to success.

Often, the real cost to doing traditional cloning is not in the DNA inputs or even the use of outside DNA synthesis services but in the fully burdened labor time expended. Design rules that reduce a biologist's expended project time can be very valuable. By amplifying a biologist's design capability without budgetary impact, TeselaGen's design rules increase a biologist's productivity by reducing the time it takes to design new DNA.

Along with design rule capture and cost optimization, assembly protocol optimization is also built in to TeselaGen. For example, unique to TeselaGen is the ability to recognize when pieces of DNA are incompatible with one another. Biologists trying to make a new construct with modern techniques may have DNA pieces that tend to assemble in the wrong order. With TeselaGen, these assembly incompatibilities can be identified and workarounds suggested. Biologists working by

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hand would be hard pressed to identify and then address these types of problems accurately and time efficiently without TeselaGen.

Scar-less Assembly

Traditional cloning, including relatively recent innovations such as MoClo or BioBrick™ style cloning, cannot control every DNA base pair in the final construct and one always end up with internal assembly control sequences called scar sequences. With TeselaGen, biologists can always produce scar-less DNA allowing for the accumulation and reuse of intermediate constructs during DNA construction.

Scar sequences also affect DNA performance. Putting together ten pieces of DNA implies ten scar sequences. It has recently become very clear that control over every DNA base pair is extremely important and introducing uncontrolled scar sequences can easily impact DNA efficacy. This is especially true for companies making enzymes, antibodies, or any types of proteins. Any scar sequences in the middle of a protein coding sequence may destroy its functional. By providing high fidelity, scar-less DNA constructs, TeselaGen releases the biologist from the harmful impact of scar sequences.

Unique Capability

TeselaGen is the only available scar-less DNA design and assembly system that can automatically and comprehensively construct and manage the combinatorial libraries required to implement modern screening and directed evolution efforts. For many sophisticated constructs, it may be the only system available which can automatically provide an assembly protocol. Moreover, because TeselaGen produces assemblies that are scar-less, it can also reuse its DNA inputs over and over again in the assembly process. While BioBricks and MoClo provide some functionality for creating combinatorial libraries, those methodologies produce scared sequences impacting the usefulness of the final result.

Because traditional cloning is limited to restriction site availability, it typically ceases being effective between ten and twenty kilobases with most biologists assembling DNA less than ten kilobase in length. Moreover, there is always the chance that a final DNA construct may be unattainable given the precursors being used. TeselaGen has no such limitation and is able to construct DNA on the scale of microbial genomes that are typically one to ten megabases in length. TeselaGen's more modern cloning methodologies releases biologists from the restrictions of traditional cloning allowing them to synthesize DNA that may not be possible by other means.

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Conclusion

TeselaGen is the only DNA design and assembly protocol generation service that decouples DNA from its underlying assembly protocol. By embracing a wide selection of modern scar-less cloning techniques, integrating the pricing and delivery capabilities of outside synthesis services, supporting protocol optimization and design rules, or creating the combinatorial libraries the project requires, TeselaGen gives the biologist the widest possible latitude in assembling DNA in the most cost and time efficient manner possible; in some cases the only way possible. To find out more how TeselaGen can successfully contribute to your DNA design and assembly challenges, please visit our website at http://www.teselagen.com or email us at info@teselagen.com.

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