# Slonomics™- Industrialized Gene Synthesis

## A Novel Technology Using Programmable Base Triplet Assembly

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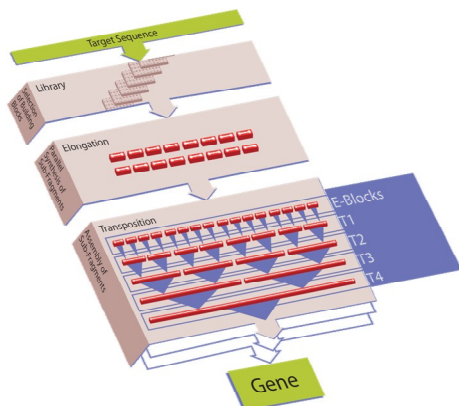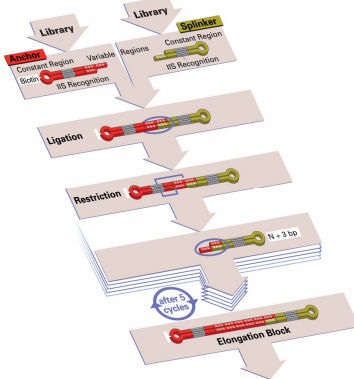*[1]CyBio Robotics, D-72127 Kusterdingen, Germany*
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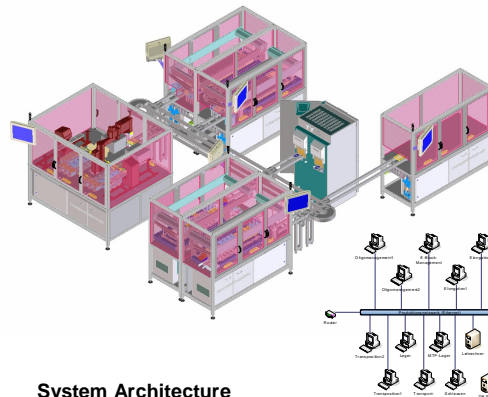
### Introduction

The synthesis of genetic constructs via the Slonomics™ technology utilizes various liquid handling, mixing, incubation and microplate handling procedures, performed via a multistep, convergent synthesis protocol. For the automated parallel production of such custom gene constructs, we developed a modular system architecture consisting of independently operating robotic stations.

### The Slonomics™ Gene Synthesis Technology

The Slonomics™ gene synthesis technology utilises a library of universal double-stranded DNA building blocks (referred to as 'anchors' and 'splinkers'). These pre-assembled oligonucleotides which form a specific secondary structure can be easily processed with DNA modifying enzymes, such as restriction endonucleases or ligases. The Slonomics™ process is based exclusively on highly standardised reaction cycles, regardless of the gene construct being synthesised. This enables the complete transfer of every working step to an industrial-style robotic platform.





*The Slonomics™ Process: Synthesis of E-Blocks and Genetic Contructs.*



### System Architecture

In order to achieve an efficient and highly robust production process, the complexity of the system was reduced by distributing the overall functionality to independent robotic stations, which are dedicated to the specific sub processes of the recursive synthesis:

- The library management for the cooled storage of approx. 5,000 oligonucleotide building blocks, and for their compilation into oligo sets,
- The synthesis of sub-sequences of the target molecule out of the building blocks, using repetitive ligation and restriction steps (Elongation),
- The assembly of the sub-sequences to the desired target molecules, using a convergent restriction and ligation process (Transposition).
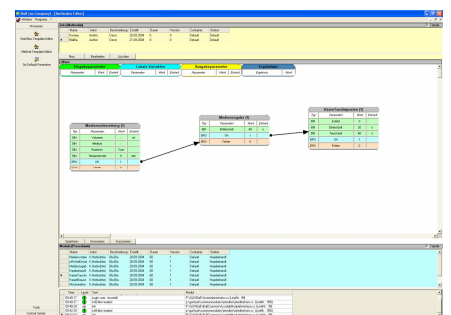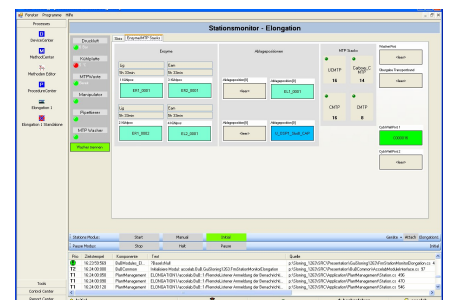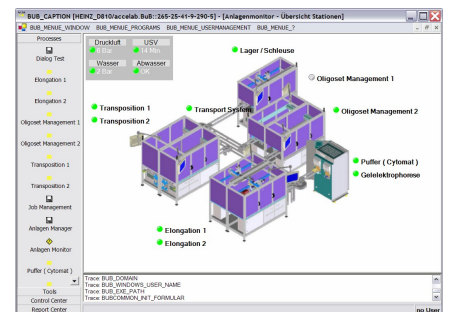


Besides the stand-alone operation of the robotic stations, which is primarily used for process development and specialty synthesis, a fully integrated operation mode is used to carry out hundreds of syntheses in parallel utilizing an automated double-belt conveyor system for the microplate transfer steps. To exploit the full capacity of the scalable system, the synthesis jobs are dispatched continuously, resulting in a continuous flow of genetic constructs, which can be collected in the commissioning station. The layered software architecture allows the graphical programming of branched processes and workflows, including the dynamic management of resyntheses.

### Workflow Management

The architecture of the accelab Workflow Manager system software is optimized to integrate components from various laboratory technology and industrial automation suppliers. At the same time, it must handle a large number of individual processes and samples efficiently within short time frames.

Therefore, proven components for data management (object oriented database), visualization (SCADA system), and device control (PLC) are used. Processes can be graphically programmed according to the ISA95 standard, thus allowing sophisticated error management strategies by definition of branched processes. All sample and process data is stored in real time.

Within the hierarchical architecture of the software, the overall workflow management coordinates the sub-processes in between the stations and allocates them to the available hardware ressources. Time-critical process sequences are handled by the local station scheduling, respectively.







*Workflow Manager Sofware: Overall System Control Center, Station Monitor for the Elongation Station, Graphical Process Editor.*