expanded the repertoire of triple-forming sequences but did not completely remove this limitation.

It was recently shown that during homologous recombination promoted by RecA a triple-stranded DNA intermediate was formed. Such a structure is a new form of the triple helix. In sharp contrast with the "classical" triplexes their third strand is parallel to the identical strand of the Watson-Crick duplex. We denote this structure as "parallel" triplex. Recently, the parallel triplex was obtained only by deproteinization of joint molecules generated by recombination proteins.

We first obtained experimental (chemical probe, melting curves and fluorescence due binding) results that provide convincingly evidence for protein-independent formation of parallel triplex [1] and than confirmed this fact by FTIR data [2]. Because the parallel triplex can be formed for any sequence, it might be "ideal" potential tool for sequence specific recognition of DNA. Unfortunately, low stability of parallel triplexes prohibits practical application of these structures.

Earlier we found that propidium iodide stabilizes selectively the parallel triplexes [3]. This fact was the basis of new approach to stabilization of parallel triplexes being developed by us now. The approach consists in use of targeting oligonucleotide, which contains in internucleotide linkage the alkyl insert coupled with intercalated ligand through linker. Length of linker was chosen to allow ligand to intercalate in the same stacking-contact (length of linker was picked by molecular dynamic calculations).

Preliminary study showed that presence of intercalating inserts increase considerably stability of DNA duplexes [4]. Now we are investigating in detail effect of such modification of targeting oligonucleotides on stability of parallel triplexes.

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Advanced Automated Sequencing Technology: Fluorescent Detection for Multiplex DNA Sequencing

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Automation of a large-scale sequencing process based on instrumentation for automated DNA hybridization and detection is a focal point of our research. Recently, we have devised a method for amplifying fluorescent light output on nylon membranes by using an alkaline phosphatase-conjugated probe system combined with a fluorogenic alkaline phosphatase substrate [1]. The amplified signal allows sensitive detection of DNA hybrids in the sub-femtomole/band range.

On the basis of this detection chemistry, automated devices for detecting DNA on blotted microporous membranes using enzyme-linked fluorescence, termed Probe Chambers, have been built. The fluorescent signal is collected by a CCD camera operating in a Time Delay and Integration mode. Concentrated solutions of probes and enzymes are stored in Peltier-cooled septa sealed vials and delivered by syringe pumps residing in a gantry style pipetting robot. Fluorescence excitation is generated by a mercury arc lamp acting through a fiber optic "light line". Three 30 x 63 centimeter sequencing membranes can be simultaneously processed, currently revealing up to 108 lane sets per multiplex cycle. A probing cycle is completed approximately every eight hours.

Integration of the Probe Chamber into the production pipe line is accomplished through connections to the laboratory data base. A critical component of a high-throughput sequencing laboratory is the software for interfacing to instrumentation and managing work flow. The Informatics Group of the Utah Genome Center has designed and implemented an innovative system for automating and managing laboratory processes. This software allows the model of workflow to be easily defined. Given such a model, the system allows the user to direct and track the flow of laboratory information. The core of the system is a generic, client-server process management engine that allows users to define new processes without the need for custom programming. Based on these definitions, the software will then route information to the next process, track the progress of each task, perform any automated operations, and provide reports on these processes. To further increase the usefulness of our laboratory information sys-