

Genetic Algorithm for the Design of Microchip Flow Cytometers

Hyunwoo Bang^{*}, Yunsil Heo^{**}, Won Gu Lee^{*}, Hoyoung Yun^{*}, Jung Ki Min^{*},
Jun Keun Chang^{***} and Dong-Chul Han^{*}

^{*}School of Mechanical and Aerospace Engineering,

Seoul National University, Seoul 151-742, Korea, savoy@snu.ac.kr

^{**}Department of Design | Media Arts, UCLA, LA, CA 90095-1456, USA

^{***}Digital Bio Technology, Inc., Seoul 151-742, Korea

ABSTRACT

The design of a microchannel can evolve through the genetic algorithm (GA), a digital Darwinism. We adopted the GA while optimizing two types of commercial microchip flow cytometers. One detects signal with spatial imaging in a single channel and the other detects fluorescence intensity of particles with a spot laser in a flow focusing channel. Using the GA, we optimized the detailed wall geometry with the former, and the design of channel network with the latter. The GA has been implemented to run in parallel on multiple computers connected via XML-RPC protocols using JAVA and SQL database technology.

Keywords: genetic algorithm, microchannel, design optimization, microchip flow cytometer

1 INTRODUCTION

Partly due to its short history of the lab-on-a-chip industry, design problems have been solved by trial and error dictated by design specifications and guided by the experience and intuition of the engineer. The GA was selected to stochastically guide the algorithm through the solution space of available designs and arrive at an evolved one. It is a Darwinian “survival of the fittest” approach employed to search for optima in large multidimensional spaces [1, 2]. GAs permit virtual entities to be created without requiring an understanding of the procedures or parameters used to generate them. The measure of success or fitness of each individual can be calculated automatically.

It is convenient to use the biological terms genotype and phenotype when discussing artificial evolution. In biological systems, a genotype is usually composed of DNA and contains the instructions on how organism is to be developed. In the GA a genotype is a coded representation of a possible individual or problem solution. In our case, a genotype is a series of design variables for the microchannel geometry (Figure 1). GAs typically use populations of genotypes consisting of strings of binary digits or parameters. These are read to produce phenotypes which are then evaluated according to some fitness criteria and selectively reproduced. New genotypes are generated by copying, mutating, and/or combining the genotypes of

the most fit individuals, and as the cycle repeats, the population ascends to higher and higher levels of fitness. There are several components of the physical simulation used in this work: heuristic rigid body dynamics, numerical integration, collision detection, collision response, friction, and viscous fluid effects. The GA has been implemented to run in parallel on multiple computers connected via XML-RPC protocols using JAVA and SQL database technology.

2 OPTIMIZATION PROCEDURES

We adopted the GA while optimizing two types of commercial microchip flow cytometers. One detects signal with spatial imaging in a single channel and the other detects fluorescence intensity of particles with a spot laser in a focusing channel network (Figure 1). The former drives a drop of whole blood sample through its single narrow microchannel (6 microns in width, 2 microns in depth) and analyzes the bright field and fluorescence morphology of the blood cells by real-time image processing [3]. And the latter introduces hydrodynamic flow focusing using sheath fluids [4]. Cells are injected into the core of the sheath flow and confined to a narrow single-file stream by hydrodynamic focusing. As fluorescent labeled cells flow past a focused laser beam, they generate light scattering and fluorescence emission measured by optics and electronics. Using the GA, we optimized the detailed wall geometry of the former, and the design of channel network of the latter.

There are other reasons for us to choose two types of microchannels for this optimization. With the first one, we tried to prove the fact that a microsystem can evolve through the GA, a digital Darwinism. Because this device uses visual inspection, when the cells are inside a microchannel they should be sparsely distributed and should not be close together which will result in erroneous data acquisition [3]. By optimizing its channel geometry, the GA for this one was aimed at maximizing the distances between these blood cells while they are passing through the microchannel. In this case, fitness evaluation of the GA becomes a rather simple form which considers only one parameter: “distance between each cell.” The newly optimized microchannel was fabricated and compared with the existing one.

And with the second one, we've constructed a novel framework for the microchannel design optimization. This can simulate the GA with multiple goals. In our case, these goals include higher detection throughput, better signal purity, larger signal intensity and lower sheath consumption. We programmed a JAVA software which can compute a final goal from the combination of these requirements for the optimization to meet the specific need of the user. A user can notify his/her particular design intention to the software through the graphical user interface by distributing priority scores of each requirement. The requirements are allocated to multiple fitness evaluation routines independently and each routine assesses the microchannel design currently in simulation with respect to its assigned goal. So the overall fitness evaluation of the GA becomes a complex one which computes weighted sum of many fitnesses.

Both types of optimization are implemented to run in parallel on multiple computers connected via XML-RPC protocols using JAVA and SQL database technology. A server computer schedules the process of the genetic algorithm. It sets current population of genotypes in a database and farms them out to the other computers to be fitness tested, and gathers back the fitness values after they have been determined. The fitness tests are the dominant computational requirement of the system. Performing a fitness test per processor is a simple but effective way to parallelize this genetic algorithm, and the overall performance scales quite linearly with the number of processors. Our parallel implementation has several merits by using the latest web technologies. One is that it is developed as a web applet. It means that anyone who can access the internet through any kinds of web browsers can participate in our project by just visiting our web page. With this publicity, our parallel implementation gets rid of the burden of economical and computational cost for massive calculation loops. Second is that the program is based on JAVA which means that it can be run on any systems including Windows, MAC OS, Solaris or even on OSs for cellular phones and PDAs as the motto of JAVA says "write once, use everywhere."

Processing IDE (Integrated Development Environment) was used for the JAVA programming environment. Processing is an open project initiated by Ben Fry (Broad Institute) and Casey Reas (UCLA Design | Media Arts) [5]. Processing evolved from ideas explored in the Aesthetics and Computation Group at the MIT Media Lab. The choice of Processing is that it is a fully object-oriented language and environment based on JAVA technology which can easily implement particles and the microchannels as virtual objects. Object-oriented programming (OOP) paradigm is an excellent choice when intuitively simulating real-world phenomenon in a programming language. Moreover the powerful networking of JAVA helped us to easily setup parallel implementation of the algorithm's massive calculation loops.

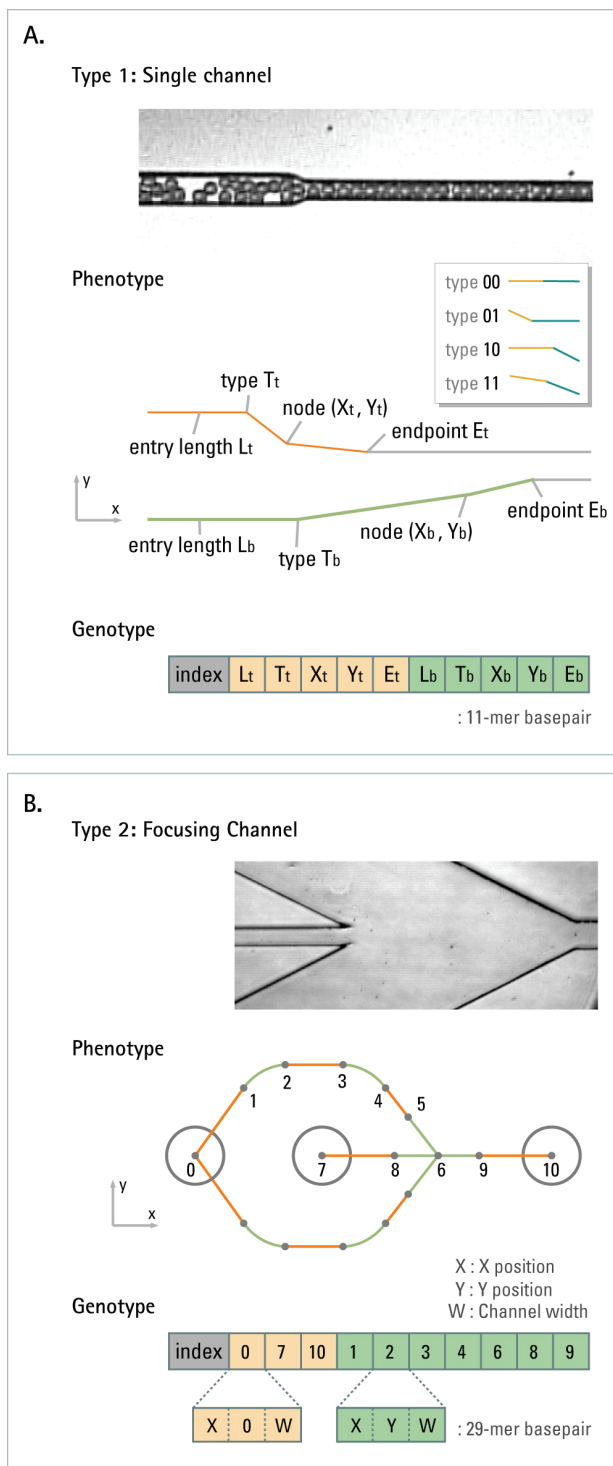


Figure 1: The genotype and the phenotype of the microchannel designs (A: single channel with detailed wall geometry, B: focusing channel network).

3 RESULTS

With the first type of microchip, the final evolution was performed using 20 species of 5,000 genomes. The average fitness of the individuals of each species is inspected over 75 generations. The rate of evolutionary progress was similar for all species. All species took about 30 generations before they reached their plateau and the populations of each species converged toward homogeneity. Through the evolution process, the fitness values increased with about 40% of their initial values on average. The design parameters such as the skewness (difference in the lengths to the ends of wedges) of the nozzle and slopes of the wedge segments were monitored through the evolution processes. Some examples of optimized microchannel morphologies (evolution tree) are shown in Figure 2.

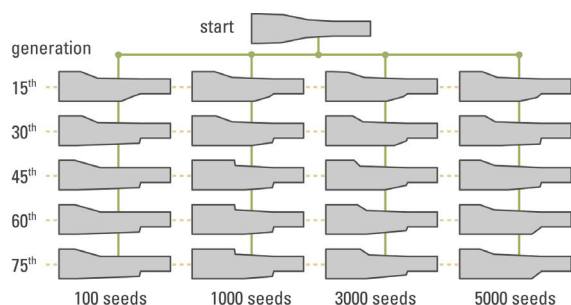


Figure 2: The evolutionary tree for the microchannel optimization

The newly optimized microchannel was fabricated and compared with the existing one (Figure 3). RBCs flowed through both the existing and newly fabricated microchannels. The comparison between these two microchannels clearly proves the enhancement of the newly fabricated one. As in Figure 3, RBCs in the newly fabricated microchannel are more sparsely distributed in observation channel without generating doublets of RBCs.

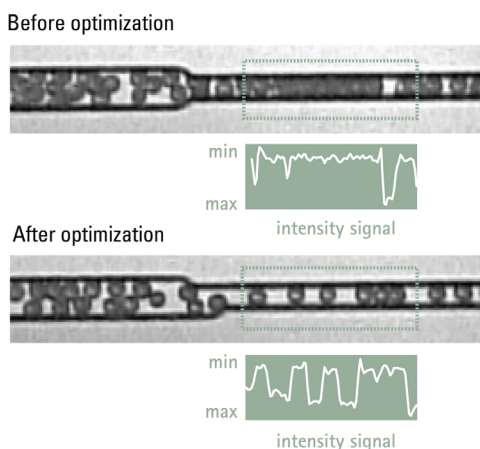


Figure 3: Optimization results

For the second type of microchip, a stand-alone JAVA software has been developed and distributed to multiple PCs. Each PC became a member of a computing cluster and served as a client for a host computer. On the host computer users can tweak current combination of optimization goals. The host computer broadcasts the current optimization goal and the client PCs update their objectives. In Figure 4, you can see screen shots of host and client softwares. With this setup, we could also supervise and direct the overall simulation not to fall into a trivial solution or a local minima by monitoring its current status of evolution.

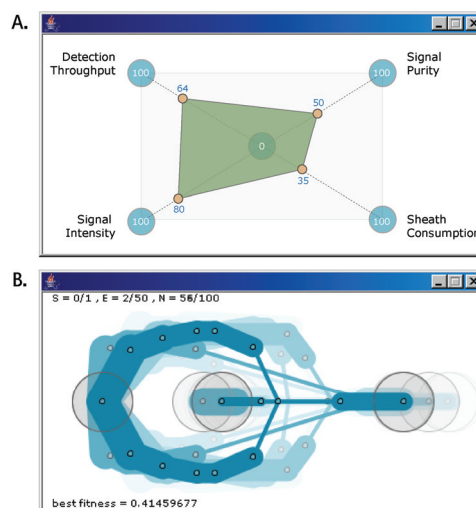


Figure 4: Screen shots of the developed software (A: host-side, B: client-side)

4 DISCUSSIONS

The proposed methodologies can be extended to resolve more complex design problems. By implementing simulations such as microchannel mixing, electro-osmosis and multiphase flows, this method will be applicable to even handling various microchannel design problems. This kind of optimization for microchip design will make new solutions, consequently enhancing microchip devices. At the same time, it will give creative hints as to how we can overpass existing obstacles in designing microsystems in the industry. We strongly believe that this kind of evolutionary processes for the microchip design will provide breakthroughs while optimizing microchip devices and give creative clues for jumping over existing obstacles in the industry. That is how the human races have survived thorough the great challenges from the nature.

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