

# The Evolution of Cellular Computing: Nature's Solution to a Computational Problem

**Laura F. Landweber**

Ecology & Evolutionary Biology  
Princeton University  
NJ 08544-1003 USA  
LFL@princeton.edu  
www.princeton.edu/~lfl

**Lila Kari**

Department of Computer Science  
University of Western Ontario  
London, ON, N6A 5B7 Canada  
lila@csd.uwo.ca  
www.csd.uwo.ca/~lila

## ABSTRACT

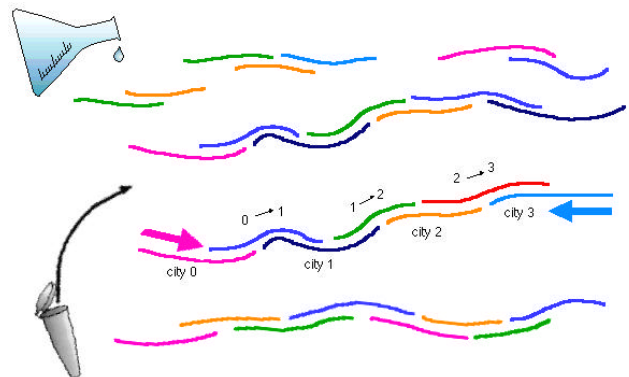
How do cells and nature 'compute'? They read and 'rewrite' DNA all the time, by processes that modify sequences at the DNA or RNA level. In 1994, Adleman's elegant solution to a seven-city Directed Hamiltonian Path problem using DNA (Adleman 1994) launched the new field of DNA computing, which in a few years has grown to international scope. However, unknown to this field, two ciliated protozoans of the genus *Oxytricha* had solved a potentially harder problem using DNA several million years earlier. The solution to this problem, which occurs during the process of gene unscrambling, represents one of nature's ingenious solutions to the problem of the creation of genes. RNA editing, which can also be viewed as a computational process, offers a second algorithm for the construction of functional genes from encrypted pieces of the genome.

## 1. Gene Unscrambling as a Computational Problem

### 1.1. Introduction

Ciliates are a diverse group of 8000 or more unicellular eukaryotes (nucleated cells) named for their wisp-like covering of cilia. They possess two types of nuclei: an active *macronucleus* (soma) and a functionally inert *micronucleus* (germline) which contributes only to sexual reproduction. The somatically active macronucleus forms from the germline micronucleus after sexual reproduction, during the course of development. The genomic copies of some protein-coding genes in the micronucleus of hypotrichous ciliates are obscured by the presence of intervening non-protein-coding DNA se-

quence elements (internally eliminated sequences, or *IESs*). These must be removed before the assembly of a functional copy of the gene in the somatic macronucleus. Furthermore, the protein-coding DNA segments (macronuclear destined sequences, or *MDSs*) in *Oxytricha* species are sometimes present in a permuted order relative to their final position in the macronuclear copy. For example, in *O. nova*, the micronuclear copy of three genes (Actin I, -telomere binding protein, and DNA polymerase) must be reordered and intervening DNA sequences removed in order to construct functional macronuclear genes. Most impressively, the gene encoding DNA polymerase (DNA pol) in *O. trifallax* is apparently scrambled in 50 or more pieces in its germline nucleus (Hoffman and Prescott 1997). Destined to unscramble its micronuclear genes by putting the pieces together again, *O. trifallax* routinely solves a potentially complicated computational problem when rewriting its genomic sequences to form the macronuclear copies.



**Figure 1: DNA hybridization in a molecular computer.** PCR primers are indicated by arrows.