## **Biochemical identification of prime numbers**

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**Summary** A biochemical technique is proposed whereby prime numbers may be identified. © 1999 Harcourt Publishers Ltd

Adleman (1) and Lipton (2) have given good examples of solving computational problems with the use of molecular solutions and tools from molecular biology. The advantage of these biochemical systems over conventional computation is based on the huge number of molecules and actions occurring in solutions. This overcomes, the relative lower velocity of biochemical molecular interactions.

Using a similar idea, the identification of prime numbers may be possible through synthesis of oligo and polynucleotides by aggregation of small units of oligonucleotides. Polymers with a total number of units corresponding to prime numbers will be absent in the universe of polynucleotides formed by aggregation of dimers, trimers, tetramers and so on, induced by a ligase enzyme, for instance a T4 bacteriophage ligase (3,4).

The synthesis of oligo and polynucleotides can be performed in different vials, with each one containing dinucleotides, trinucleotides, tetranucleotides, etc. plus enzyme, ATP, MgCl, Tris-HCl and BSA. In each vial, after an appropriate incubation time, at 22°C, polynucleotides will be formed with a total number of nucleotides corresponding to multiplets of the starting units of oligonucleotides, lacking those polynucleotides with a number of elements equal to prime numbers.

So, for instance, after incubation, in the vials containing dinucleotides, trinucleotides, tetranucleotides, pentanucleotides and hexanucleotides, there should be found the starting oligonucleotides plus polynucleotides formed by aggregation of oligo units, but not the heptanucleotide composed by a prime number of units, seven in this case.

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For identification of the formed oligo and polynucleotides of different length, it is possible to take advantage of the fast and accurate technique of capillary electrophoresis, which differentiates oligo and polynucleotides of different size with high precision (5). It will probably be necessary to cut big polynucleotides using restriction enzymes and then identify the different fractions so obtained, then calculating the real length of the original polymer.

The oligonucleotides of different total length necessary to build up, by addition, the respective polymers, can be obtained by chemical synthesis or by biochemical methods, e.g. hydrolyzing polynucleotides and isolating the fractions of different length by electrophoresis. Eventually these can be amplified by the PCR technique.

In the case of enzymatic oligomerization (ligase action) of small polynucleotides, the ligase activity could be accelerated by the use of complementary templates able to be paired with the small oligonucleotides, thus facilitating the ligase action (6).

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