An Improved Immune Algorithm for Protein Folding  
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Introduction
This work is about solving the protein structure prediction (PSP) problem which is concerned with predicting the 3D native conformation of a protein from the corresponding 1D amino acid sequence. It is postulated that the native conformation corresponds to the global minima of the free energy; hence the PSP problem can be considered as an optimisation problem.

The clonal selection algorithm (Cutello et al., 2007) is a state of art algorithm for this problem. In this work new, immune inspired, operators have been incorporated to improve the clonal selection algorithm’s performance.

Clonal Selection Algorithm and the Biological Immune System
The clonal selection algorithm is an optimisation algorithm based upon the clonal selection principle in the biological immune system. The clonal selection principle describes the response of cells from the adaptive immune system, called lymphocytes, to antigens. Lymphocytes are divided into T cells and B cells. When a B cell is exposed to an antigen it recognises it begins to proliferate (clone). The clones terminate as either antibody secreting plasma cells or B-memory cells that circulate throughout the host in case of re-infection. The clones undergo mutation of the gene region responsible for recognising antigens; this allows the immune system to adapt to recognise new antigens (de Castro & Timmis, 2002).

Immune Cell Diversity and the Mixed Strategy Operator
The biological immune system is made up of many types of cell that work both co-operatively and competitively. Examples of immune cells are macrophages, neutrophils, natural killer cells, phagocytes, plasma cells, T, cells, TH cells and CD8+ T cells all of which perform different functions.

The mixed strategy operator is based upon the cell diversity in the immune system. Which crossover or mutation technique is used to create offspring depends on a probability distribution

\[ p \text{Hypermutation} + (1-p) \text{Macromutation} \]

The mixed strategy operator helps overcome the large energy barriers between minima and exploration of the search space away from the current minima.

The archive operator is inspired by immune memory. A memory, or archive, of minima similar to one that it has (de Castro & Timmis, 2002)

\[ P_{\text{archive}}(i) = \sum_{j=1}^{n} P_{\text{hypermutation}}(i) P_{\text{hypermutation}}(j) \]

The archive operator helps overcome the large energy barriers between minima that are too similar.

The mixed strategy operator helps overcome the large energy barriers between minima by encouraging population diversity and exploration of new areas of the search space.

Conclusions
The new operators improve the clonal selection algorithm’s success of finding the lowest known energy value and reduce the number of energy function evaluations used to find it. This is because the mixed strategy operator allows for large jumps that tune between minima and the archive operator encourages diversity and exploration of the search space away from the current minima.

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