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# Particle swarm optimization based estimation of HIV-1 viral load in resource limited settings

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**Viral load (VL) testing is highly important for diagnosis and staging of HIV-1 infection and for initiating antiretroviral treatment in AIDS patients. However, due to the cost and availability of viral load testing instruments, VL testing is not being performed in many developing and underdeveloped countries. Such countries depend on CD4 tests as an alternative. In this work, a method for estimating the HIV-1 viral load from CD4 cell counts, using Particle Swarm Optimization (PSO) technique was proposed. The efficiency of the proposed method was evaluated using error analysis and correlation analysis. The average error in estimation of HIV-1 viral load was found to be 3.317%. Further, an average correlation value (R) of 0.99 was found between the actual and estimated values of HIV-1 viral load. This work seems to be of high clinical significance, since efficient and low cost strategies for estimation of HIV-1 viral load is required for proper diagnosis and staging of the disease.**

**Key words:** HIV/AIDS, viral load, CD4 cells, particle swarm optimization.

## INTRODUCTION

At present, the World Health Organization (WHO) guidelines recommend routine use of viral load (VL) testing, since HIV-1 infection cannot be effectively diagnosed without viral load testing (Greig et al., 2011; Calmy et al., 2007). Further, Viral load testing is the only definitive method for early detection of Anti Retroviral Treatment (ART) failure (Kantor et al., 2009).

However, VL testing has not been routinely implemented in many resource-limited settings due to cost, availability and accessibility of testing instruments. Also, VL testing is complex, making its application in resource-limited settings challenging (Greig et al., 2011). Even if equipment to determine VL is available, a single VL test is very expensive and costs $50-$160 US Dollars (Koenig et al., 2006).

Implementation of commercial HIV-1 viral load assays requires high-cost equipment such as thermal cyclers, highly skilled personnel, and expensive reagents which is not suitable for resource-limited settings (Fiscus et al., 2006). Further, VL is commonly assessed by measuring plasma HIV RNA levels, however the use of nucleic acid based VL assays in many resource-constrained settings are susceptible to viral DNA contamination (Greengrass et al., 2009).

Routine monitoring of viral load and CD4 cell counts has been adopted in well resourced settings since the use of a combination of both the tests provides more information on the risk of disease progression than does the use of CD4 test alone. However, resource constrained environments use only CD4 tests for staging the disease since simple, less expensive and automated equipment for measurement of CD4 cell count is available (Balakrishnan et al., 2011; Mermin et al., 2011). The dynamic three dimensional mathematical model of

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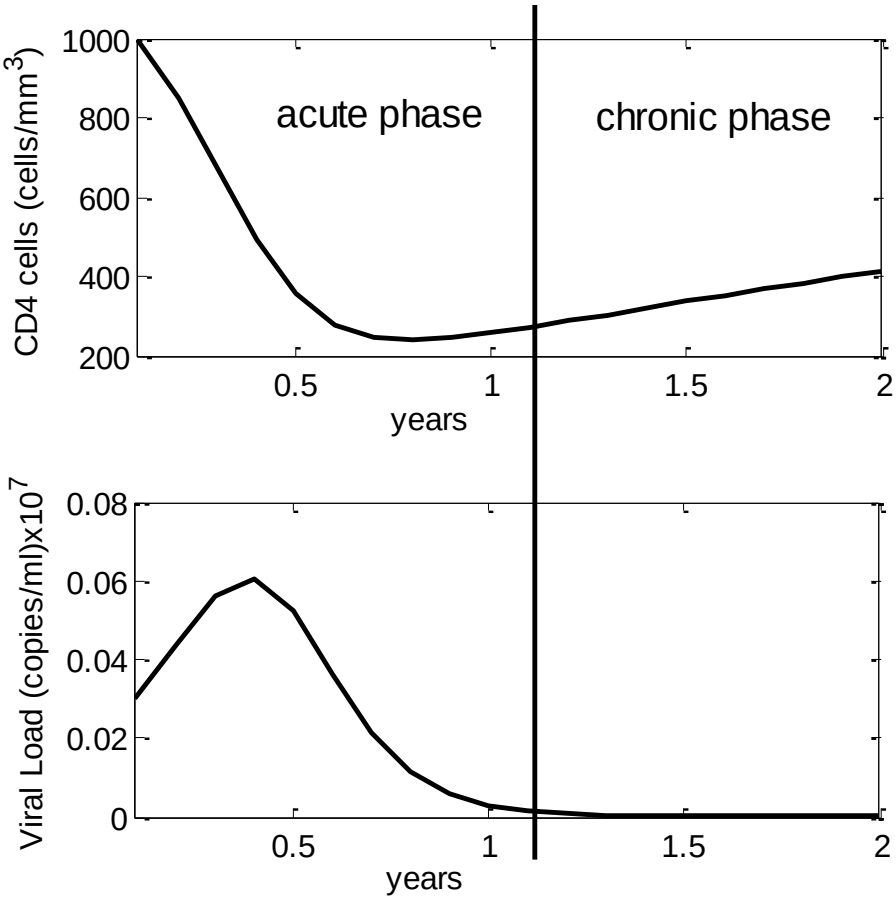


**Figure 1.** The acute and chronic stages of HIV-1 infection shown as a function of time.

the HIV system describes the interaction of HIV with the patient's immune system. The dynamics of the model includes the response of the CD4 lymphocyte population, the CD8 lymphocyte population and the HIV-1 viral load and is characterized by first order nonlinear differential equations (de Souza, 1999).

Swarm Intelligence is the property of a system in which the collective behavior of simple quasi-independent agents, locally interacting with their environment, causes global intelligent behavior to emerge. Swarm intelligence techniques have been widely used for solving hard estimation problems since they are robust, flexible, fault tolerant, scalable, and highly parallelizable (Da San Martino et al., 2006; Kennedy and Eberhart, 2001; Consoli et al., 2008; Kamalanand and Jawahar, 2012).

The objective of this work was to efficiently estimate HIV-1 viral load from CD4 cell count using a computational swarm intelligence technique known as the Particle Swarm Optimization (PSO) technique in conjunction with the three dimensional HIV model. In this paper, the preliminary analysis on the possibility of using PSO for viral load prediction is presented. The efficiency of the proposed method has been assessed using error analysis, correlation analysis and time taken for estimation of HIV-1 viral load.

## MATERIALS AND METHODS

In this work, an attempt has been made to estimate the HIV-1 viral load from CD4 cell count in the acute and chronic phase of the HIV-1 infection. In the acute stage of the disease, the probability of a HIV patient infecting his/her partner is very high since the HIV-1 viral load increases rapidly in this stage. Further, a typical evolution of CD4 cell count and HIV-1 viral load in the acute and chronic phase of the disease is presented in Figure 1.

### *The three dimensional HIV model*

The response of the concentrations of the CD4 lymphocyte population, the CD8 lymphocyte population and the HIV-1 viral load can be characterized by the following first order nonlinear differential equation (de Souza, 1999; Filter et al., 2005; Ho and Ling, 2010).

$$\frac{dx(t)}{dt} = a(x_0 - x(t)) - bx(t)z(t) \quad (1a)$$

**Table 1.** Description of HIV model parameters.

| Parameter | Description |
|---|---|
| a | death rate of CD4 cells |
| b | rate of infection of CD4 cells by virus |
| c | death rate of CD8 cells |
| d | rate of increase of CD8 cells in response to increased viral load |
| e | rate of increase of viral load |
| f | rate of decrease of viral load |

$$\frac{dy(t)}{dt} = c(y_0 - y(t)) + dy(t)z(t) \quad (1b)$$

$$\frac{dz(t)}{dt} = z(t)(ex(t) - fy(t)) \quad (1c)$$

Where, x(t), y(t) and z(t) are the concentrations of the CD4 lymphocyte population, the CD8 lymphocyte population and the HIV-1 viral load, respectively. $x_0$ and $y_0$ are the normal unperturbed concentrations of the CD4 and CD8 lymphocyte population. a, b, c, d, e and f are the system parameters. The description of each parameter (Sam Ge, 2005) is provided in Table 1.

***Particle Swarm Optimization***

Particle Swarm Optimization (PSO) is a form of swarm intelligence in which the behavior of a biological social system like a flock of birds or a school of fish is simulated (Kennedy and Eberhart, 2001). For an optimization problem with *d* variables, each particle *i* of the swarm S = {1, 2,…..,s} has an associated position vector $x_i$ = ($x_{i1}$, $x_{i2}$, ….,$x_{ij}$,….,$x_{id}$) and its corresponding velocity vector $v_i$ = ($v_{i1}$,…..$v_{ij}$,…..,$v_{id}$). The coordinates of a particle, represents an individual solution of the optimization problem. The final solution is obtained as the set of trial solutions converges towards the optimal solution due to the foraging group dynamics of the swarm of particles.

Each particle i of the swarm communicates with a subset of S that can vary dynamically. Each particle keeps and uses information of its better position during the process search. Also it can obtain the best position reached among the particles of its social neighborhood, which can be the whole swarm or a part of it. The information of the best positions influences the behavior of particles. In all the cases the value of the objective function is also stored.

The initial positions and velocities of particles are obtained randomly. In the computer code, the initial set of particles is obtained using a random number generator. At every iteration, the particles update their position and velocity by means of recurrent equations. The position of the particle is modified using exclusively its velocity. However, in updating of its velocity, the value of its own velocity, the best position of the particle ($b_i$), and the best position of the group of particles of the swarm ($g_i$), is taken into account. These best positions act with different weights, like centers of attraction for particles. The vector equations to update the position $x_i$ and velocity $v_i$ of each particle of the swarm can be described as

$$v_i = c_1 v_i + c_2 \eta(b_i - x_i) + c_3 \eta(g_i - x_i) \quad (2)$$

$$x_i = x_i + v_i \quad (3)$$

The parameter $c_1$ represents the effect of the inertia whose mission is to control the magnitude of the velocity to avoid its indefinite growth. The values $c_2$ and $c_3$ are the weights that represent the degree of confidence of the particle. η refers to a random number with uniform distribution in [0, 1] that is independently generated each time (Castro et al., 2009).

For estimating the HIV-1 viral load, the CD4 cell count data consisting of twenty time points (N=20) for a total period of two years was used. The PSO program was developed in such a way that it estimates all the six parameters of the three dimensional HIV/AIDS model so that the HIV-1 viral load could be obtained. The objective function that needs to be minimized for estimation of HIV/AIDS model parameters and hence the HIV-1 viral load, is described by Equation (4).

$$J_\theta = \sum_{n=1}^{N} \frac{(\hat{x}_n - x_n)^2}{N \ mean(x_n)} \quad (4)$$

where, $\theta = [a, b, c, d, e, f]$ is the set of HIV parameters to be estimated; $x$ represents the CD4 cell population; N is the total number of samples available for CD4 data.

In this work the value of the parameters $c_1$, $c_2$ and $c_3$ were set to 0.721, 1.193 and 1.193 respectively. The estimation was performed using Matlab 7.0.1 on a computer with 1.73 GHz processor. Further, the PSO algorithm for estimating the HIV-1 viral load from CD4 cell count is presented.

**Algorithm 1:** Particle Swarm optimization algorithm for estimation of HIV-1 viral load.

**Input:** Set of available measurement data of CD4 cell population.

**Output:** HIV-1 viral load.

**Begin**

**Step 1:** Initialize a population of particles with random positions and velocities on d dimensions in the problem space.

**Step 2:** For each particle evaluate the desired optimization fitness function in d variables.

**Step 3:** Compare particle's fitness evaluation with particle's pbest. If current value is better than pbest, then set pbest value equal to current value, and pbest location equal to the current location in d-dimensional space.

**Step 4:** Compare fitness evaluation with the population's overall previous best. If current value is better than gbest, then reset gbest to the current particle's array index and value.

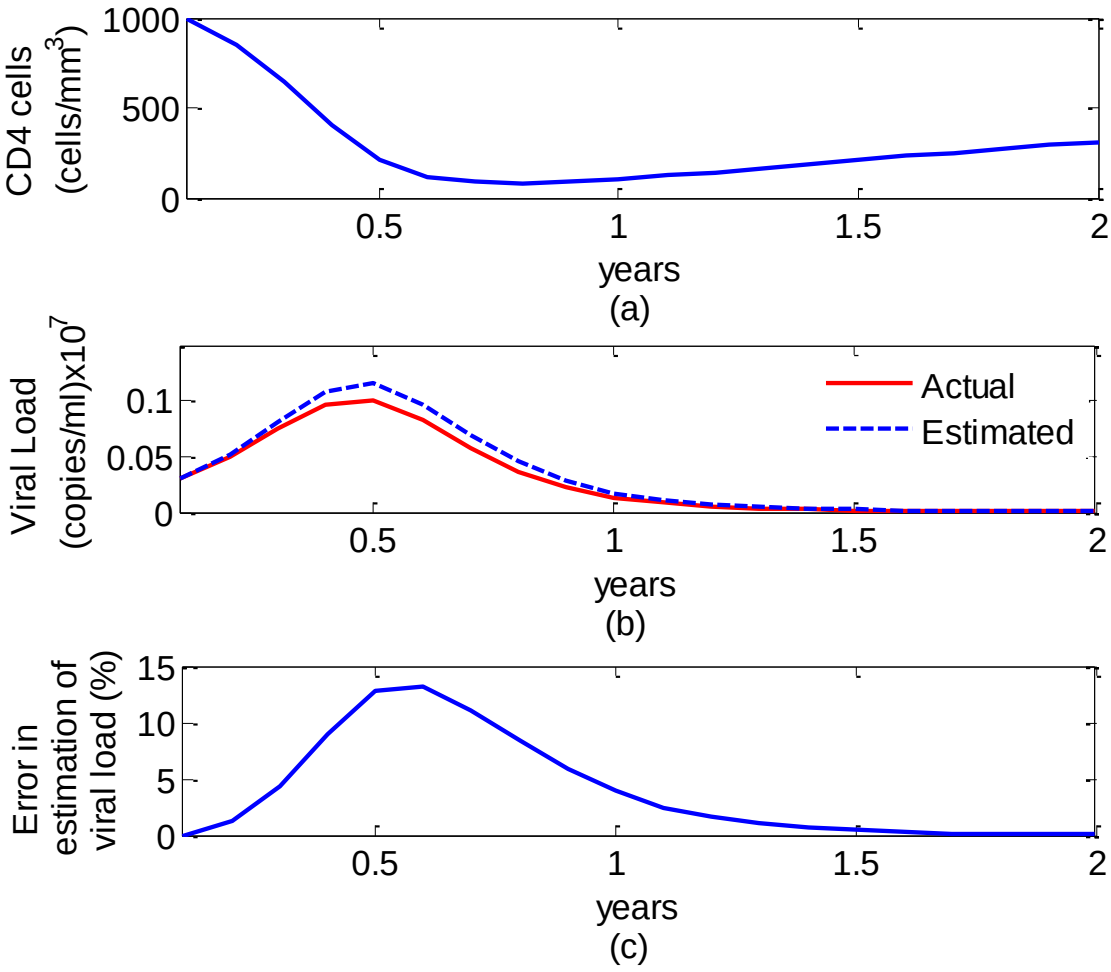


**Figure 2.** (a) The variation in CD4 cell count, (b) the actual (——) and estimated (-----) values of HIV-1 viral load and (c) the error in estimation of viral load shown as a function of time (Sampling time = 0.1 years; Number of data points = 20).

**Step 5:** Change the velocity and position of the particle according to the update equations:

$v_i = c_1 v_i + c_2 \eta(b_i - x_i) + c_3 \eta(g_i - x_i)$
$x_i = x_i + v_i$

**Step 6:** Loop to step 2 until a stopping criterion (maximum number of iterations of good fitness) is reached.

**end**

## RESULTS AND DISCUSSION

Figure 2a, b and c shows the variation in CD4 cell count, the actual and estimated values of HIV-1 viral load and the error in estimation of viral load as a function of time, respectively. For estimation, 25 particles and 50 iterations were used to balance the tradeoff between accuracy in estimation and the total estimation time. The average error in estimation of viral load was found to be 3.317%. Further, the maximum estimation error in the acute stage of the disease was found to be 14.19%, whereas, the maximum estimation error in the chronic phase of the disease was found to be 0.4399%. Hence it appears that the PSO algorithm for estimation of HIV-1 viral load is highly efficient during the chronic phase of the disease. Further, the value of actual and estimated viral load at each sampling time instant is presented in Table 2.

The correlation of actual HIV-1 viral load with the viral load estimated using particle swarm optimization technique is shown in Figure 3. In this case, a high correlation (R=0.9971) was observed between the actual and estimated HIV-1 viral load. Based on the results of the correlation analysis, it is seen that the proposed method is efficient in estimation of the HIV-1 viral load from CD4 measurements.

Further, the results of the correlation and error analysis

**Table 2.** The values of actual and estimated viral load at each sampling time, for a particular case.

| Time (years) | Actual viral load (copies/ml x $10^7$) | Estimated viral load (copies/ml x $10^7$) |
|---|---|---|
| 0.1 | 0.03 | 0.03 |
| 0.2 | 0.0501 | 0.05155 |
| 0.3 | 0.07566 | 0.08056 |
| 0.4 | 0.09732 | 0.10764 |
| 0.5 | 0.10035 | 0.11514 |
| 0.6 | 0.08199 | 0.09717 |
| 0.7 | 0.05653 | 0.06931 |
| 0.8 | 0.03552 | 0.04516 |
| 0.9 | 0.0215 | 0.02822 |
| 1.0 | 0.01301 | 0.01745 |
| 1.1 | 0.00805 | 0.0109 |
| 1.2 | 0.00515 | 0.00697 |
| 1.3 | 0.00344 | 0.00459 |
| 1.4 | 0.00239 | 0.00313 |
| 1.5 | 0.00174 | 0.00221 |
| 1.6 | 0.00131 | 0.00162 |
| 1.7 | 0.00103 | 0.00122 |
| 1.8 | 0.00084 | 0.00095 |
| 1.9 | 0.00071 | 0.00077 |
| 2.0 | 0.00062 | 0.00064 |

**Table 3.** Correlation of actual and estimated viral loads, corresponding standard deviations and results of error analysis for different cases.

| Case | R | $R^2$ | Standard deviation | Maximum error (%) | Average error (%) |
|---|---|---|---|---|---|
| 1 | 0.9910 | 0.9821 | 0.0054 | 17.41 | 5.82 |
| 2 | 0.9971 | 0.9942 | 0.0030 | 14.19 | 3.31 |
| 3 | 0.9970 | 0.9940 | 0.0031 | 13.57 | 4.21 |
| 4 | 0.9992 | 0.9984 | 0.0016 | 12.91 | 2.88 |
| 5 | 0.9932 | 0.9866 | 0.0082 | 25.06 | 5.16 |
| 6 | 0.9897 | 0.9795 | 0.0060 | 21.09 | 5.33 |
| 7 | 0.9916 | 0.9834 | 0.0037 | 19.56 | 5.56 |
| 8 | 0.9921 | 0.9842 | 0.0044 | 13.53 | 4.19 |
| 9 | 0.9891 | 0.9783 | 0.0061 | 14.50 | 4.45 |
| 10 | 0.9945 | 0.9890 | 0.0072 | 13.85 | 4.12 |

conducted on different cases are presented in Table 3. It is seen that in all the cases, a high correlation exists between the actual and estimated values of viral load. Also, the standard deviation in all the cases is found to be less than 0.01. The maximum percentage error in all cases was found to be in the acute stage of the disease. The average error in estimation of HIV-1 viral load from CD4 cell count was found to be small in all the cases (<6%). In all the cases, the results of the t-test indicate a high P value (P>0.5) between the actual and estimated HIV-1 viral load, stating that the actual and estimated values are close to each other.

Further, analysis on the PSO algorithm for estimation of HIV-1 viral load is described in Figures 4 and 5. The time taken for estimation of HIV-1 viral load using PSO is shown as a function of the number of particles, in Figure 4. It is seen that the estimation time increases exponentially as the number of particles increased. The estimation time is shown as a function of the number of iterations in Figure 5. The estimation time is found to increase nonlinearly with increase in the number of iterations. Although an increase in number of iterations results in better accuracy, the estimation time also increases. Also, increasing the number of iterations is not

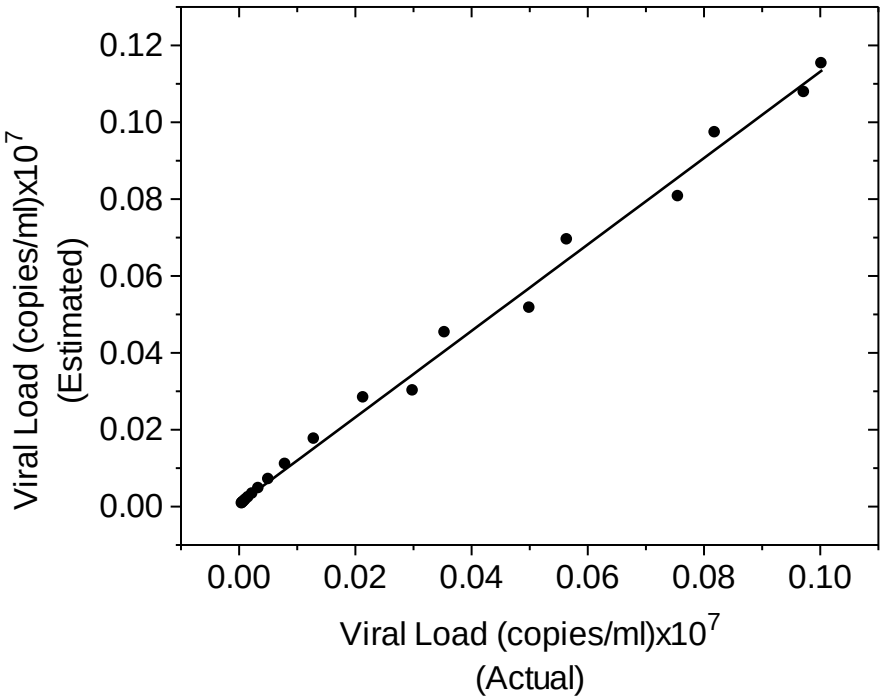


**Figure 3.** Correlation of actual HIV-1 viral load with the viral load estimated using particle swarm optimization technique, for a particular case.

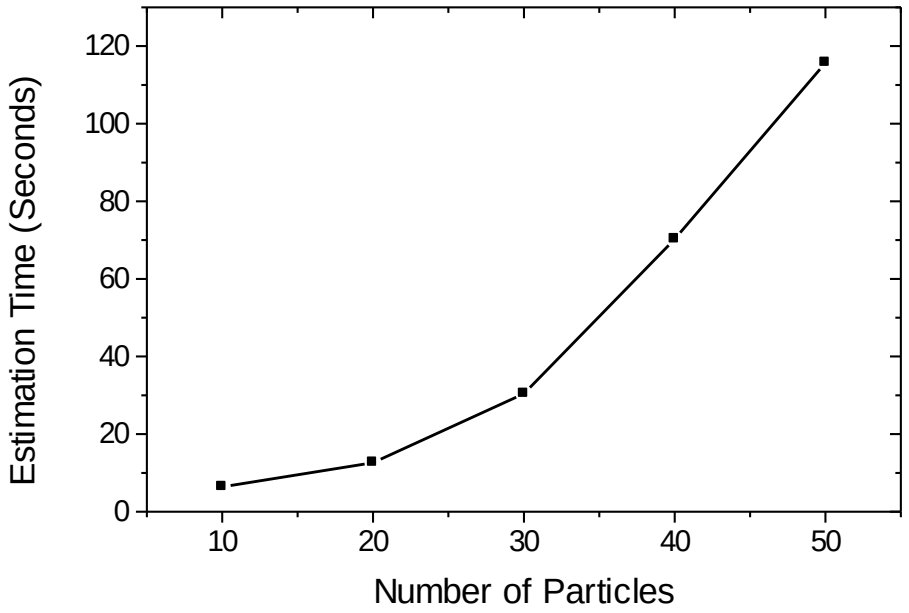


**Figure 4.** Time taken for estimation of HIV-1 viral load model using PSO, shown as a function of the number of particles (iterations = 50).

suitable when estimation algorithm is compiled on a system with low end configuration.

Further, by improving the configuration of the computer, the cost of the computer also increases. Since, this work is aimed at the estimation of HIV-1 viral load in resource limited settings, an optimal particle number of 25

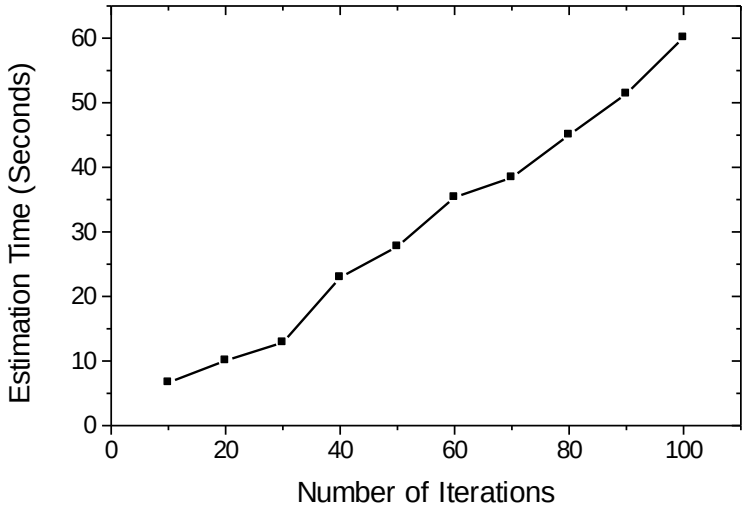


**Figure 5.** Time taken for estimation of HIV-1 viral load using PSO, shown as a function of the number of iterations (number of particles = 25).

particles and 50 iterations were used for estimation.

## Conclusions

Viral load (VL) testing is highly important for diagnosis of HIV-1 infection and for the detection of antiretroviral treatment (ART) failure in AIDS patients. However, due to the cost and availability of viral load testing instruments, VL testing is not being performed in many developing and underdeveloped countries. Such resource limited countries depend on CD4 tests as an alternative.

In this work, an efficient swarm intelligence technique known as the particle swarm optimization has been used to estimate the values of HIV-1 viral load from CD4 cell count. The estimation was performed using Matlab 7.0.1 on a computer with 1.73 GHz processor. The performance of the proposed method has been analyzed using error analysis, correlation analysis and the time taken for estimation of HIV-1 viral load.

Using PSO algorithm, the average error in estimation of HIV-1 viral load was found to be 3.317%. Further it was found that the estimation error in acute phase of the disease is more than the estimation error in the chronic phase of the disease. The time taken for estimation of viral load was found to be 120 s when 50 particles are used. Results demonstrate that the PSO technique is efficient in estimating the HIV-1 viral load from CD4 measurements. Further, the imprecise and inaccurate CD4 measurements will affect the accuracy of viral load estimation using PSO technique. Hence, accurate CD4 cell count measuring instruments are required.

This study seems to be of high clinical relevance since the resource limited estimation of HIV-1 viral load is essential for design of proper treatment strategies and for detection of ART failure for HIV infected patients in developing and underdeveloped countries.

## REFERENCES

Balakrishnan P, Iqbal HS, Shanmugham S, Mohanakrishnan J, Solomon SS, Mayer KH, Solomon S (2011). Low-cost assays for monitoring HIV infected individuals in resource-limited settings. Indian J. Med. Res. 134(6): 823–834.

Calmy A, Ford N, Hirschel B, Reynolds SJ, Lynen L, Goemaere E, Garcia de la Vega F, Perrin L, Rodriguez W (2007). HIV viral load monitoring in resource-limited regions: optional or necessary?. Clin. Infect. Dis. 44(1): 128-134.

Castro JP, Landa-Silva D, Moreno JA (2009). Exploring Feasible and Infeasible Regions in the Vehicle Routing Problem with Time Windows Using a Multi-objective Particle Swarm Optimization Approach. Studies in Computational Intelligence. 236: 103-114.

Consoli S, Moreno-Perez JA, Darby-Dowman K, Mladenovic N (2008). Discrete particle swarm optimization for the minimum labelling Steiner tree problem. Stud. Comput. Intell. 129: 313-322.

Da San Martino G, Cardillo FA, Starita A (2006). A new swarm intelligence algorithm for image alignment. Proceedings of Advances in Medical, Signal and Information Processing, 17-19 July 2006, pp. 1-4.

de Souza FMC (1999). Modeling the dynamics of HIV-1 and CD4 and CD8 lymphocytes. IEEE Eng. Med. Biol. 18: 21–24.

Filter RA, Xia X, Gray CM (2005). Dynamic HIV/AIDS parameter estimation with application to a vaccine readiness study in Southern Africa. IEEE Trans. Biomed. Eng. 52: 784–791.

Fiscus SA, Cheng B, Crowe SM, Demeter L, Jennings C, Miller V, Respess R, Stevens W (2006). HIV-1 viral load assays for resource-limited settings. PLoS Med. 3(10): e417.

Greengrass V, Lohman B, Morris L, Plate M, Steele PM, Walson JL, Crowe SM (2009). Assessment of the low-cost Cavidi ExaVir Load assay for monitoring HIV viral load in pediatric and adult patients. J. Acquir. Immun. Defic. Syndr. 52(3): 387-390.

Greig J, du Cros P, Klarkowski D, Mills C, Jørgensen S, Harrigan PR, O'Brien DP (2011). Viral load testing in a resource-limited setting: Quality control is critical. J. Int. AIDS Soc. 12: 14:23.

Ho CYF, Ling BWK (2010). Initiation of HIV therapy. Int. J. Bifurcat. Chaos. 20: 1279–1292.
Kamalanand K, Jawahar PM (2012). Coupled jumping frogs/particle swarm optimization for estimating the parameters of three dimensional HIV model. BMC Infect. Dis. 12(Suppl 1): 82.
Kantor R, Diero L, Delong A, Kamle L, Muyonga S, Mambo F, Walumbe E, Emonyi W, Chan P, Carter EJ, Hogan J, Buziba N (2009). Misclassification of firstline antiretroviral treatment failure based on immunological monitoring of HIV infection in resource-limited settings. Clin. Infect. Dis. 49:454-462.
Kennedy J, Eberhart R (2001). Swarm intelligence. Morgan Kaufmann Publishers, San Francisco, CA., pp. 287-319.
Koenig SP, Kuritzkes DR, Hirsch MS, Léandre F, Mukherjee JS, Farmer PE, del Rio C (2006). Monitoring HIV treatment in developing countries. BMJ. 332: 602–604.
Mermin J, Ekwaru JP, Were W, Degerman R, Bunnell R, Kaharuza F, Downing R, Coutinho A, Solberg P, Alexander LN, Tappero J, Campbell J, Moore DM (2011). Utility of routine viral load, CD4 cell count, and clinical monitoring among adults with HIV receiving antiretroviral therapy in Uganda: Randomised trial. BMJ. 343: d6792.
Sam Ge S, Tian Z, Lee TH (2005). Nonlinear control of a dynamic model of HIV-1. IEEE Trans. Biomed. Eng. 52: 353-361.