Towards a dynamical model of protein folding through Supersymmetric Quantum Mechanics

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Benasque, September 2019

Objetives

- Analytically analyze the protein folding process as a diffusion process.
- Construct the temporal evolution of the probability density and calculate the characteristic times of the intermediate states of the system described by a **triple well potential** - a result from molecular dynamics.
- Provide formalism for knowledge of protein folding (spectral problem).

- The diffusion process is described by the Fokker-Planck Equation (FPE) through the probability distribution.
- FPE can be written as a Schrödinger-type (SE).
- Spectral problem: Use of the Variational Method associated with Supersymmetric Quantum Mechanics (SQM) to obtain solutions of a sixth order (triple well) polynomial potential of FPE.

- The FPE which describes the temporal evolution of the probability distribution $P(x,t)$ in diffusion systems is given by:

$$\frac{\partial}{\partial t}P(x,t) = -\frac{\partial}{\partial x}[f(x).P(x,t)] + Q\frac{\partial^2}{\partial x^2}P(x,t) = L_{FP}P(x,t)$$

- **x** is the system characteristic variable, **t** is the time variable; **Q** is the diffusion coefficient and **f**(**x**) is the acting external force

$$f(x) = -\frac{d}{dx}V(x)$$

- $V(x)$ is the free energy.

- FPE solutions can be shown to be solutions of a time-independent SE,

$$\frac{d^2}{dx^2}\Psi(x) - \frac{1}{2Q}\left(\frac{f(x)^2}{2Q} + \frac{df(x)}{dx}\right)\Psi(x) = \frac{\lambda}{Q}\Psi(x)$$

- above equation is formally equal to SE.
- Ψ expanded on an orthonormal basis
  $\rightarrow$ **espectral problem !**

- The probability distribution is then given by:

$$P(x,t|x',t') = \sum_n \Psi_n(x)\Psi_n(x')e^{-\lambda_n(t-t')}$$

- The relationship between the eigenvalues is given by

$$\frac{\lambda_n}{Q} = E_n$$

- SQM has an algebraic structure given in terms of bosonic superagebra operators, (Witten, 1981);
- Simple and practical methodology that allows us to solve SE, given the relationship between the members of a **Hamiltonian hierarchy** through superalgebra, (Sukumar, 1985);
- SQM has applications in chemical, atomic and molecular physics: analytical and numerical results of exactly solvable potentials; partially solvable; isospectral; shape invariants; periodicals; non exactly soluble: Hulthén, Morse and Coulomb in 3d; potentials describing quantum confinement (H bonds); reflectionless potentials (solitons); **bistable potential (FPE)**.

- Hamiltonian factorization H_1, **first member of hierarchy** in terms of bosonic operators and ground state energy $E_0^{(1)}$

$$H_1 = -\frac{d^2}{dx^2} + V_1(x) = A_1^+ A_1^- + E_0^{(1)}$$

- the bosonic operators define the superpotencial W_1

$$A_1^{\pm} = \left(\mp\frac{d}{dx} + W_1(x)\right)$$

$$H_1 = -\frac{d^2}{dx^2} + W_1(x)^2 - \frac{dW_1(x)}{dx} + E_0^{(1)}$$

- from superalgebra we calculate the wave function

$$A_1^- \Psi = 0 \rightarrow \Psi_0^{(1)}(x) = N\, exp(-\int_0^x W_1(x')dx').$$

- From W_1 we calculate the supersymmetric Hamiltonian partner $H_2 \rightarrow$ **second member of the hierarchy** :

$$H_2 = -\frac{d^2}{dx^2} + V_2(x) = \mathbf{A_1^- A_1^+} + E_0^{(1)}$$

- Potential $V_2(x)$ satisfies

$$W_1(x)^2 + \frac{dW_1(x)}{dx} = V_2(x) - E_0^{(1)}.$$

- fatorization of H_2: new bosonic operators and its lowest energy $E_0^{(2)}$

$$H_2 = A_2^+ A_2^- + E_0^{(2)}$$

- bosonic operators define new superpotencial $W_2(x)$
- can calculate **ground state wave function**

$$\Psi_0^{(2)}(x) = N\ exp(-\int_0^x W_2(x')dx).$$

- We can build all members of the hierarchy **systematically**

$$A_n^{\pm} = \mp \frac{d}{dx} + W_n(x)$$

- ground state wave function via superalgebra

$$\psi_0^{(n)}(x) = N\ exp(-\int_0^x W_n(x')dx').$$

$$H_n = A_n^+ A_n^- + E_0^{(n)}$$

- From superalgebra we get the spectrum of H_1

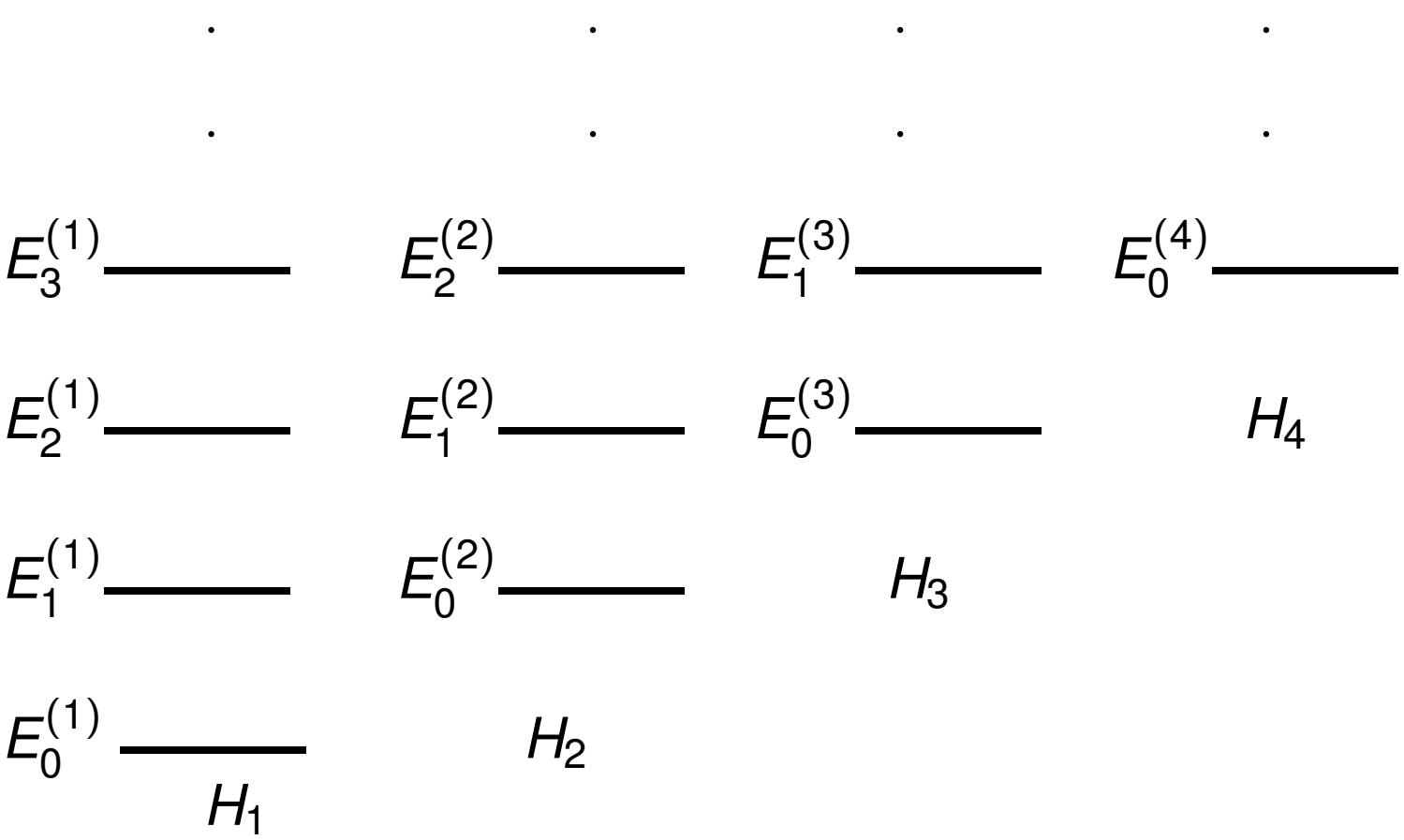
$$E_n^{(1)} = E_0^{(n+1)}$$

$$\psi_n^{(1)}(x) = A_1^+ A_2^+ ... A_n^+ \ \psi_0^{(n+1)}(x)$$

$$A_n^{\pm} = \mp \frac{d}{dx} + W_n(x)$$

- **Important: Main point is to find the superpotencial!**

- **Hamiltonian Hierarchy**



Comparing the equation coming from FPE with the SE coming from SQM for H_1

$$\frac{d^2}{dx^2}\Psi(x) - \frac{\mathbf{1}}{\mathbf{2Q}}\left(\frac{\mathbf{f(x)^2}}{\mathbf{2Q}} + \frac{\mathbf{df(x)}}{\mathbf{dx}}\right)\Psi(x) = \frac{\lambda}{Q}\Psi(x)$$

$$H_1\Psi(x) = -\frac{d^2}{dx^2}\Psi(x) + \left(\mathbf{W_1(x)^2} - \frac{\mathbf{dW_1(x)}}{\mathbf{dx}} + \mathbf{E_0^{(1)}}\right)\Psi(x)$$

$$\frac{f(x)}{2Q} = -W_1(x)\,, \quad f(x) = -\frac{dV(x)}{dx} \rightarrow \mathbf{W_1} = \frac{\mathbf{1}}{\mathbf{2Q}}\frac{\mathbf{dV(x)}}{\mathbf{dx}}$$

- $V(x)$ non-exactly solvable $\rightarrow$ Variational Method

$$V(x) = ax^6 + bx^4 + cx^2$$

- Setting notation:
  n-th state of first hierarchy member (H_1)

$$\Psi_n(x) = \Psi_n^{(1)}(x)\ , \quad \frac{\lambda}{Q} = E_n^{(1)}\ , \quad n = 0, 1, ...$$

- From one *ansatz* to the superpotencial $W(x)$, which depends on a set of free variational parameters $\{\mu\}$ we get the wave functions

$$\Psi_0^{(n)}(x) = N\ exp(-\int_0^x W_n(x')dx').$$

and calculate the minimum energy that satisfies the equation

$$E = \int \Psi_{\{\mu\}}(x')H\Psi_{\{\mu\}}(x')dx'$$

$\rightarrow$ the parameters that provide the minimum value of E numerically calculated.

$$V(x) = ax^6 + bx^4 + cx^2$$

- a, b, c constants adjusted so that we have three regions of minimum energy.
- Calculate ΔE which is the energy difference between the potential minima, E_I , E_{II} e E_{III}.
- As $V(x)$ symmetric, $E_I = E_{III}$ e $E_{II} = V(0) = 0$

$$\Delta E = E_I - E_{II}$$

Triple Well Model

$$V(x) = ax^6 + bx^4 + cx^2$$

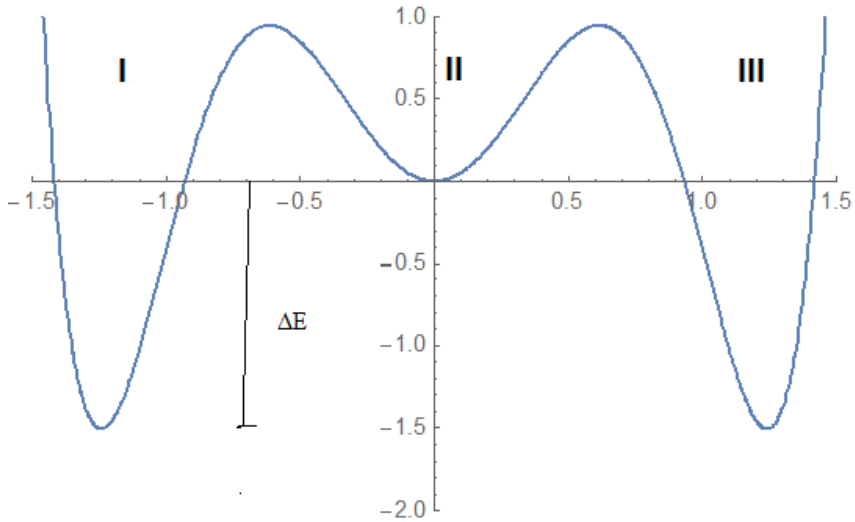


Figura: Graphics V(x) for $a = 3,10456$, $b = -8,93851$, $5,42373$, $\Delta E = -1,50737$.

$$\Delta E < 0$$

$$V(x) = ax^6 + bx^4 + cx^2$$

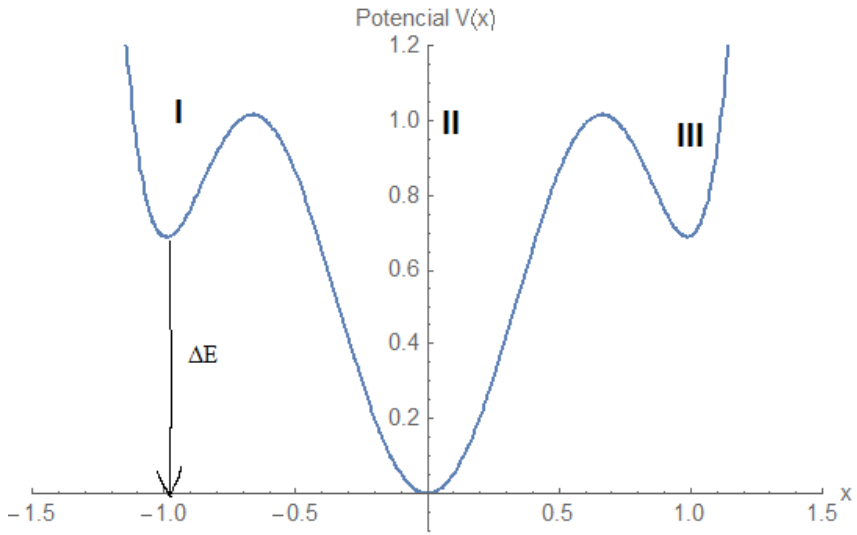


Figura: Graphics V(x) for $a = 4,20456$, $b = -8,93851$, $5,42373$, $\Delta E = 0,687984$.

$$\Delta E > 0$$

- Use of the Variational Method associated to SQM to get the ground state of all members of the hierarchy.

$$H_1 = -\frac{d^2}{dx^2} + W_1(x)^2 - \frac{dW_1(x)}{dx} + E_0^{(1)}$$

$$W_1 = \frac{1}{2Q}\frac{dV(x)}{dx} = \frac{dV(x)}{dx} = a_1 x^5 + b_1 x^3 + c_1 x$$

- a_1, b_1 e c_1 fixos; $E_0^{(1)} = 0$; $Q = 0,5$.
- Calculation of normalized ground state wave function,

$$\Psi_0^{(1)}(x) = N\ exp(-\int_0^x W_1(x')dx')$$

- Supersymmetry: Calculation of potential V_2

$$V_2(x) = W_1(x)^2 + \frac{dW_1(x)}{dx} + E_0^{(1)}$$

$$H_2 = -\frac{d^2}{dx^2} + V_2(x)$$

ansatz in the superpotential : $W_2(x) = a_2x^5 + b_2x^3 + c_2x$

$$\psi_0^{(2)}(x) = N\ exp(-\int_0^x W_2(x')dx')$$

minimizes the energy : $$\frac{< \psi_0^{(2)}(x) H_2 \psi_0^{(2)}(x) >}{< \psi_0^{(2)}(x)^2 >}$$

- $E_0^{(2)} = E_1^{(1)}$

- Up to the fifth state.
- Variational Spectrum of H_1

$$E_n^{(1)} = E_0^{(n+1)}$$

$$\Psi_n^{(1)}(x) = A_1^+ A_2^+ ... A_n^+ \ \Psi_0^{(n+1)}(x)$$

Table : Values of constants a, b and c for V (x) for the ground state and for each energy minimization. Also presented are the energy eigenvalues obtained for each minimized state.

$\Delta E = -4.10295$				
State	Eigenvalue (λ_n)	a	b	c
Ground State	0	2.60456	-8.93851	5.42373
1^0	0.244506	11.546	10.5075	-5.80739
2^0	1.16813	16.6788	-4.18534	7.73954
3^0	8.98132	9.71857	5.10745	7.88574
4^0	17.9561	4.71362	8.62217	10.0175
5^0	29.1379	4.15023	8.7174	12.3472

Table : Values of constants a, b and c for V (x) for the ground state and for each energy minimization. Also presented are the energy eigenvalues obtained for each minimized state.

$\Delta E = -1.50737$				
State	Eigenvalue (λ_n)	a	b	c
Ground State	0	3.10456	-8.93851	5.42373
1^0	0.312683	2.42861	15.8284	-6.08953
2^0	1.30144	14.9103	-5.79003	8.01573
3^0	9.04884	8.93933	3.49636	7.46396
4^0	17.4256	6.21037	6.53995	9.29638
5^0	27.7566	4.97331	7.6344	11.3683

Table : Values of constants a, b and c for V (x) for the ground state and for each energy minimization. Also presented are the energy eigenvalues obtained for each minimized state.

$\Delta E = 0.202274$				
State	Eigenvalue (λ_n)	a	b	c
Ground State	0	3.80456	-8.93851	5.42373
1^0	0.88974	4.14612	12.634	-5.52889
2^0	1.83636	12.8004	-4.50228	7.41107
3^0	9.12777	7.57855	3.63698	7.16339
4^0	17.2129	5.33955	6.15575	9.01325
5^0	27.2229	4.29561	7.08439	11.0089

Table : Values of constants a, b and c for V (x) for the ground state and for each energy minimization. Also presented are the energy eigenvalues obtained for each minimized state.

$\Delta E = 0.851968$				
State	Eigenvalue (λ_n)	a	b	c
Ground State	0	4.40456	-8.93851	5.42373
1^0	1.93928	3.97185	9.46288	-4.12221
2^0	3.04118	8.87689	-1.95067	6.32676
3^0	9.56802	5.27242	3.7141	6.72933
4^0	17.1992	3.8503	5.35477	8.53797
5^0	26.6429	3.22646	5.97482	10.3528

Table: Values of ΔE obtained for each value of the constant a adopted in potential V(x) of FPE.

a	ΔE	a	ΔE
2.50456	-1.42208	3.50456	-0.35584
2,60456	-1.38847	3.60456	-0.14664
2.70456	-1.35648	3.70456	0.03847
2.80456	-1.32593	3.80456	0.20227
2.90456	-1.29669	3.90456	0.34719
3.00456	-1.89843	4.00456	0.47529
3.10456	-1.50737	4.10456	0.588371
3.20456	-1.1633	4.20456	0.75467
3.40456	-0.59237	4.40456	0.851968
		4.50456	0.918454

- To characterize the diffusion process through FPE solutions: Calculation of the particle population (N)

$$N(t) = \int_a^b P(x,t)dx$$

- The limits of integration refer to the investigation region of the particle population.

- Remembering that from the spectrum of H_1 calculate $P(x,t)$

$$P(x,x_0,t) = \sum_n \Psi_n(x)\Psi_n(x_0)e^{-\lambda_n t}$$

- Calculation performed for each potential, each ΔE $\rightarrow$ they were 21 (Mathematica 11.3)

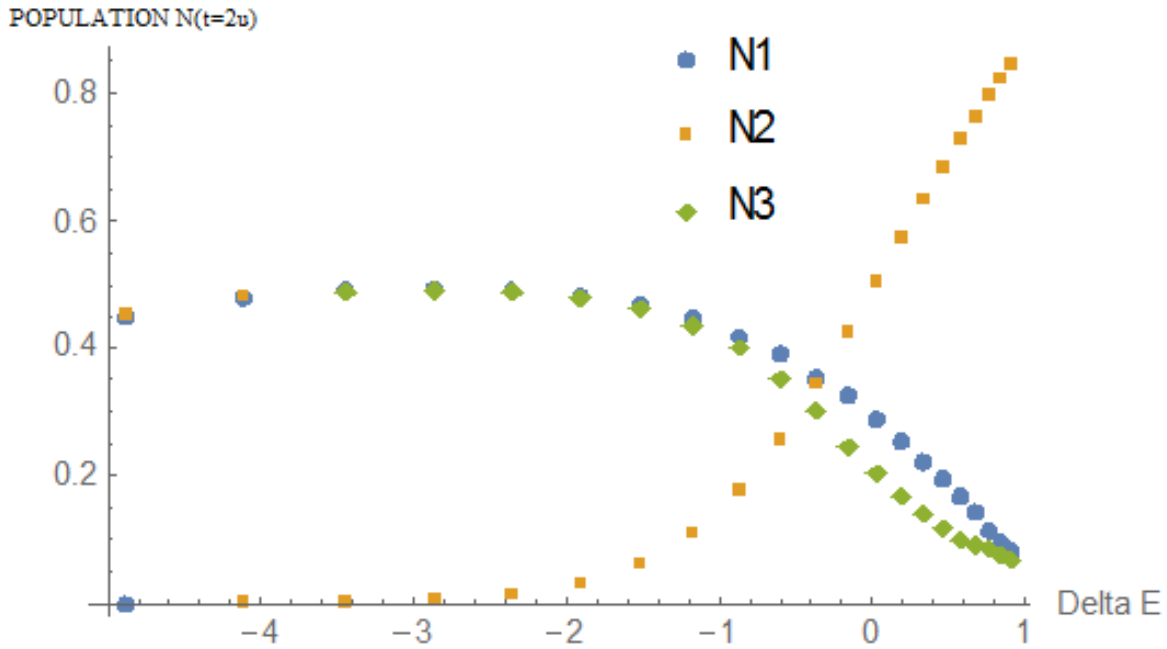


Figura: Graphic N(t=2) xΔE : Values of the particle population for each region of the potential $V(x)$ versus ΔE, time t = 2u in distribution P(x,t).

- For $\Delta E < 0$ there is equilibrium of the populations between the lateral minima; population at central minimum is null. The system behaves as if there are only two minima of energy.
- For $\Delta E > -2$ the central minimum becomes relevant and close to $\Delta E = 0$ the concentrations of the three minima are closer.
- For $\Delta E > 0$ the central minimum is larger and the population on the lateral minima decreases; there seems to be greater trapping in the central region.

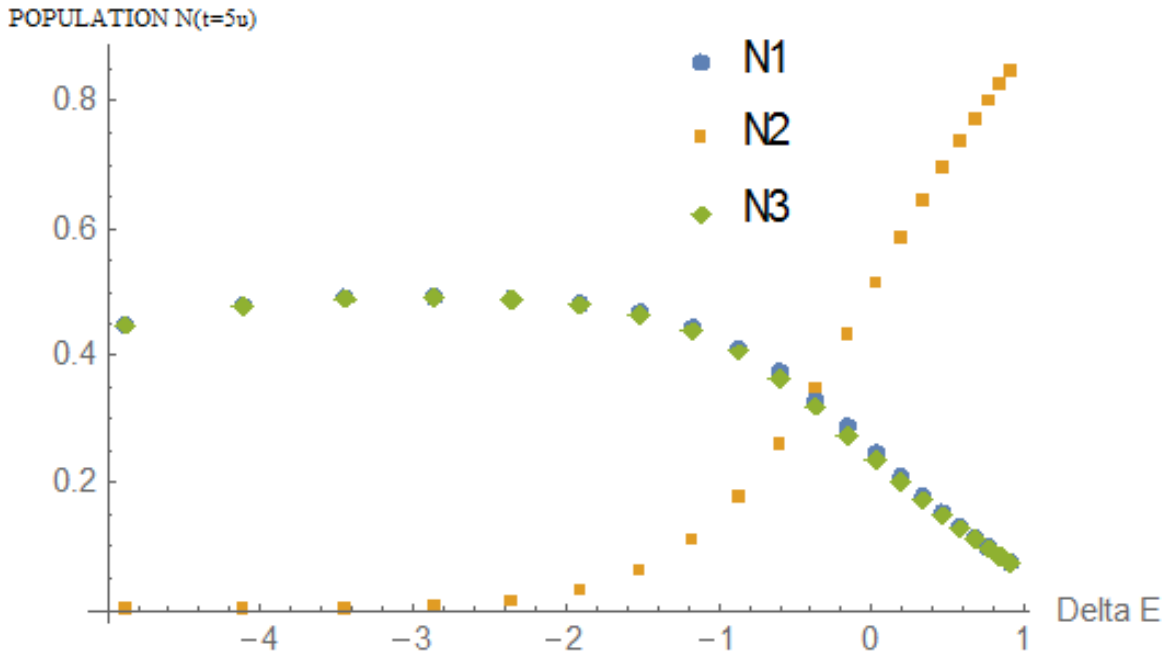


Figura: Graphic N(t=5) xΔE : Particle population values for each region of the potential $V(x)$ versus ΔE, time t = 5u in the distribution P(x,t).

- In case $t = 5u$ the distribution is in stationary state, with reference to the previous graph with $t = 2u$.
- For values of $\Delta E < 0$ between -1 and 1 the lateral minima curves are closer.
- For this value of time the system achieved a uniform distribution and a larger number of particles migrated to region III.

- To characterize the population as a function of time, choose potential with similar minimum energy, $\Delta E \sim 0$, and evaluate $N_1(t)$, $N_2(t)$ and $N_3(t)$.

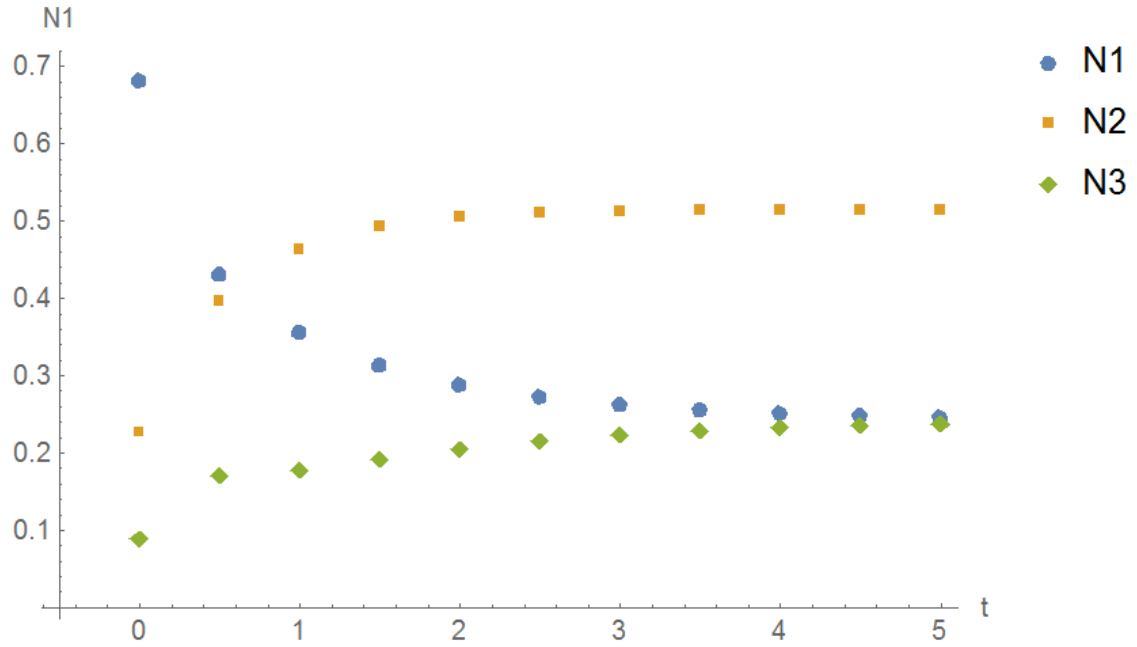


Figura: Graphic: Values of the population in Regions I, II and III versus time (t) for $a = 3.70456$ and $\Delta E = 0.03847$.

- To evaluate the characteristic time of the difusion process, τ , calculate the difference $\Delta N(t) = N_1(t) - N_3(t)$.

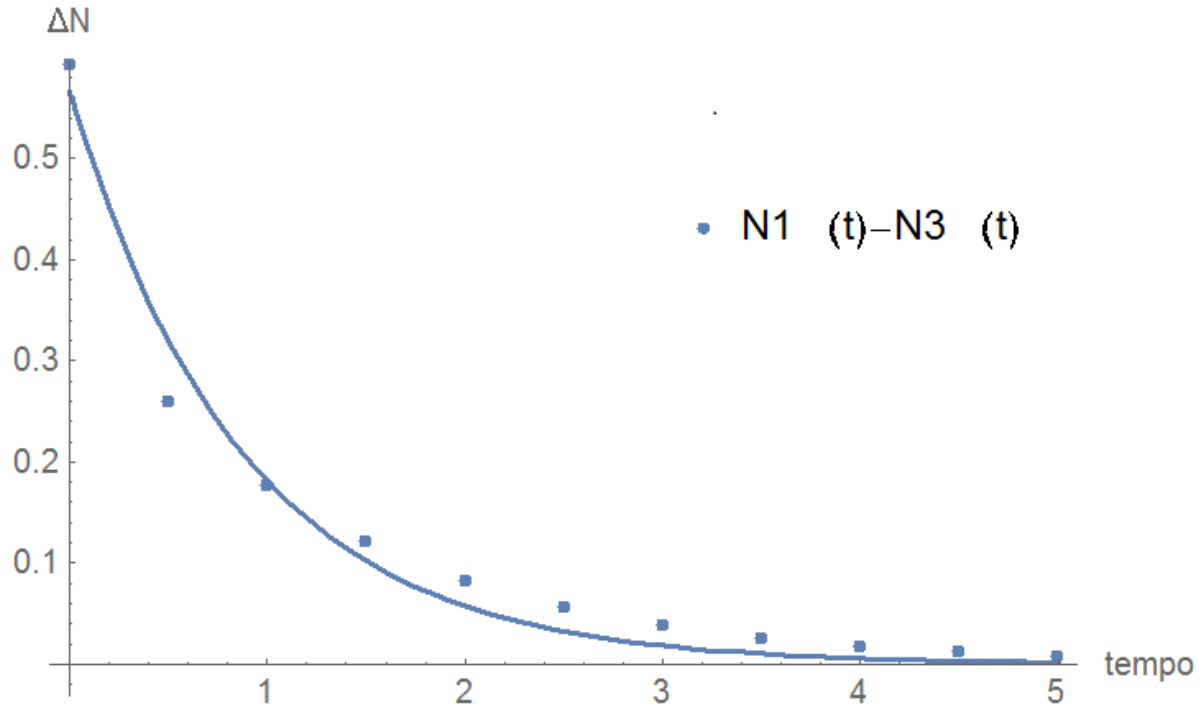


Figura: Graphic: Values of the variation of population between regions I and III for different values of time (t) for $a = 3.70456$ *and* $\Delta E = 0.03847$.

- Plot the best fitting: $\Delta N(t) \sim e^{-t/\tau}$, $\tau = 0.88u$.

Conclusions

- $\Delta E < 0$, population in central minimum is negligible.
- $\Delta E \sim 0$, population in the 3 minima are almost the same.
- $\Delta E > 0$, central minimum traps more particles.
- Calculations are in course. Need to investigate the sensitivity of the characteristic time with respect to the initial position x_0.

Thank you!