Theoretical Approaches to BioInformation Systems

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Kink solitons and breathers in microtubules

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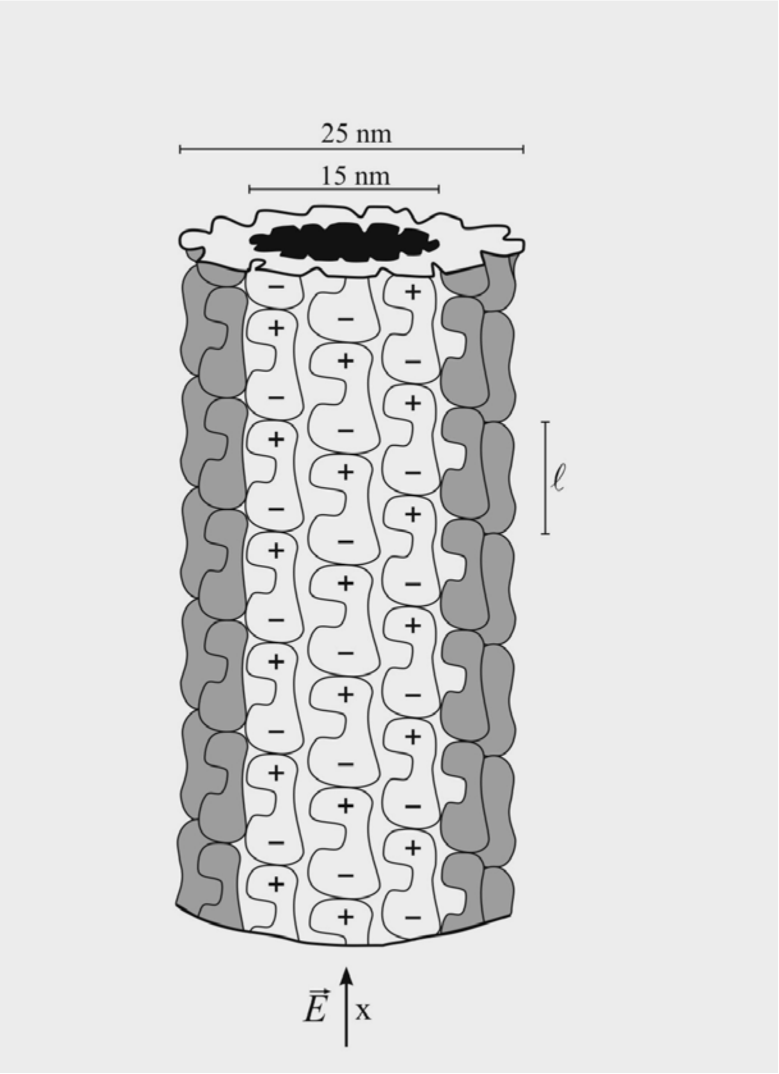
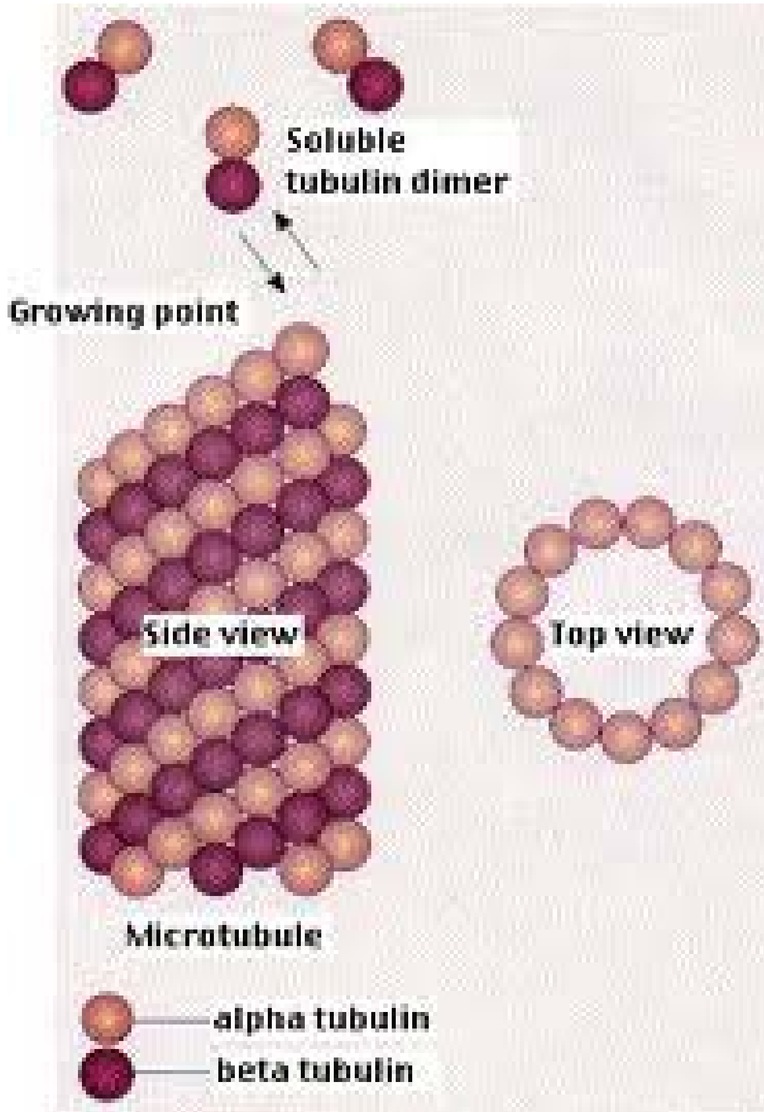
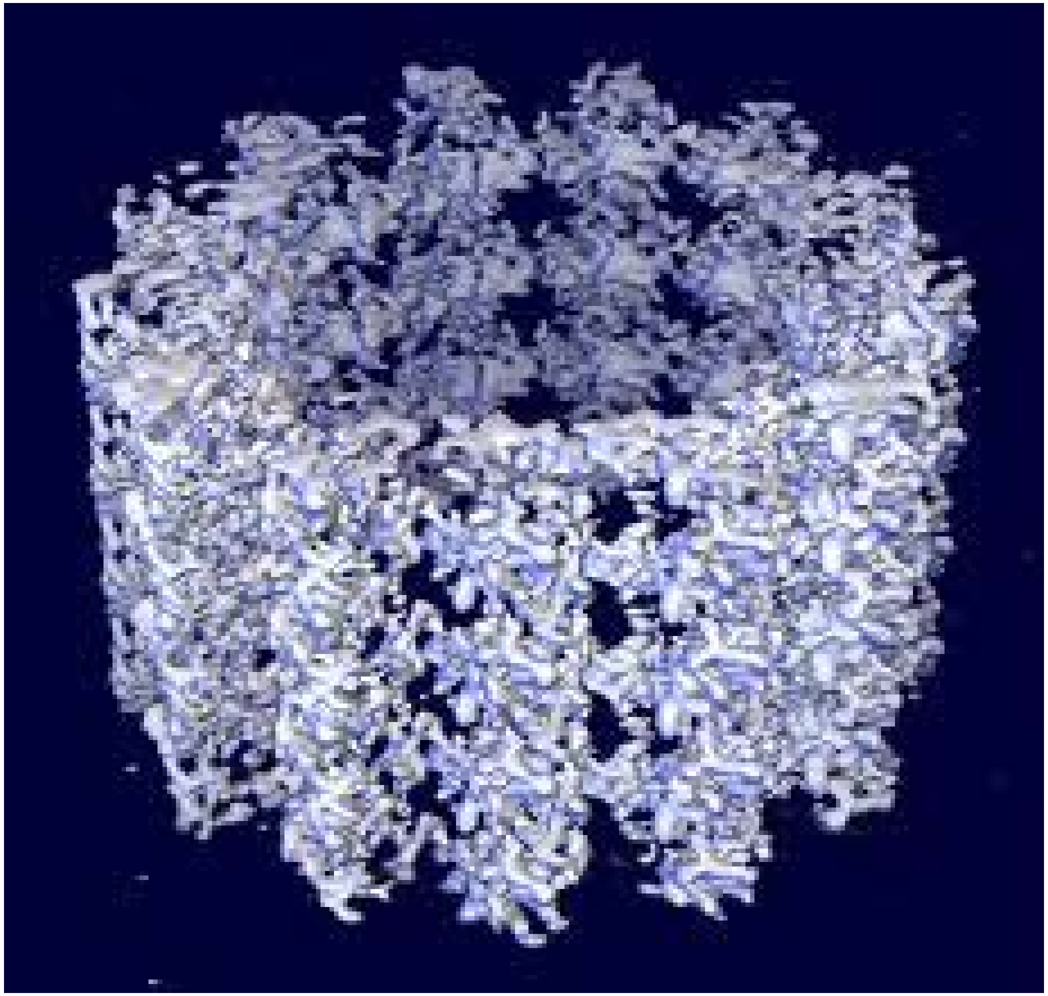
Content

1. What are microtubules?
2. Two models
3. Two approximations
4. Kinks and breathers
5. Further research

1. What are microtubules?




Soluble
tubulin dimer
Growing point
Side view
Top view
Microtubule
alpha tubulin
beta tubulin



Why are MTs important?

Microtubules are important cell protein structures.

a) Cytoskeleton

b) Network for motor proteins

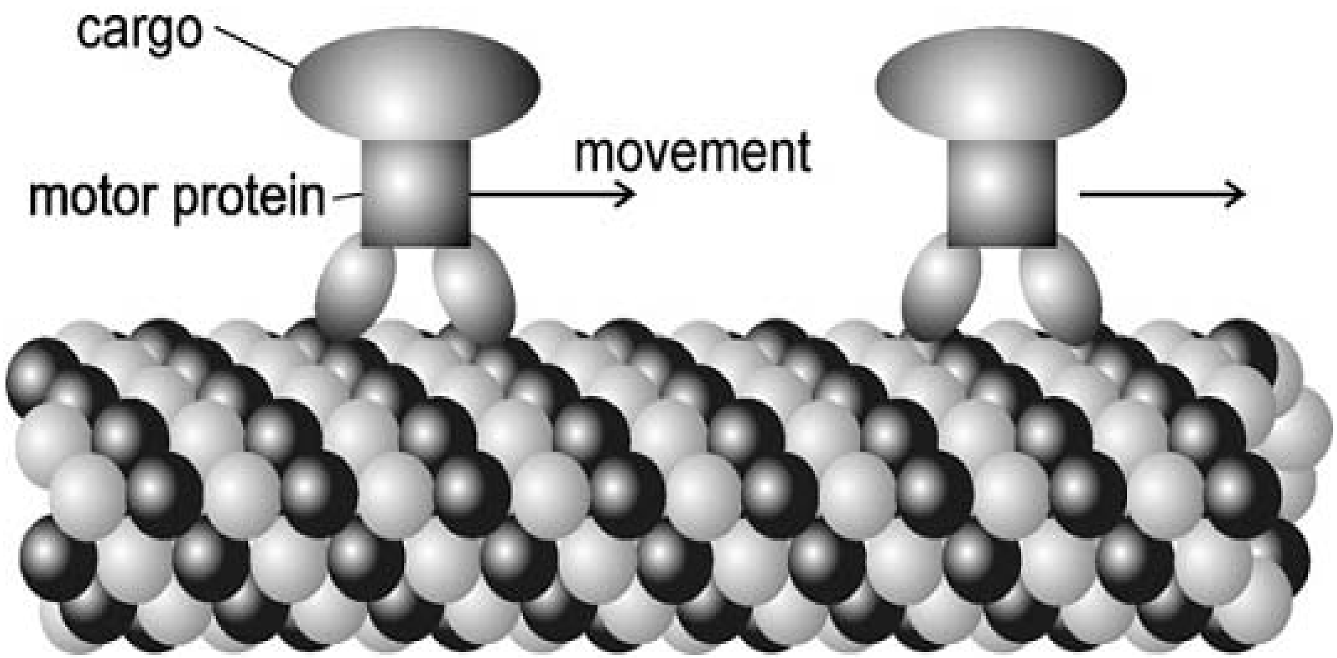


Fig. 3. Movement of the motor proteins on the microtubule, cargo not in scale.

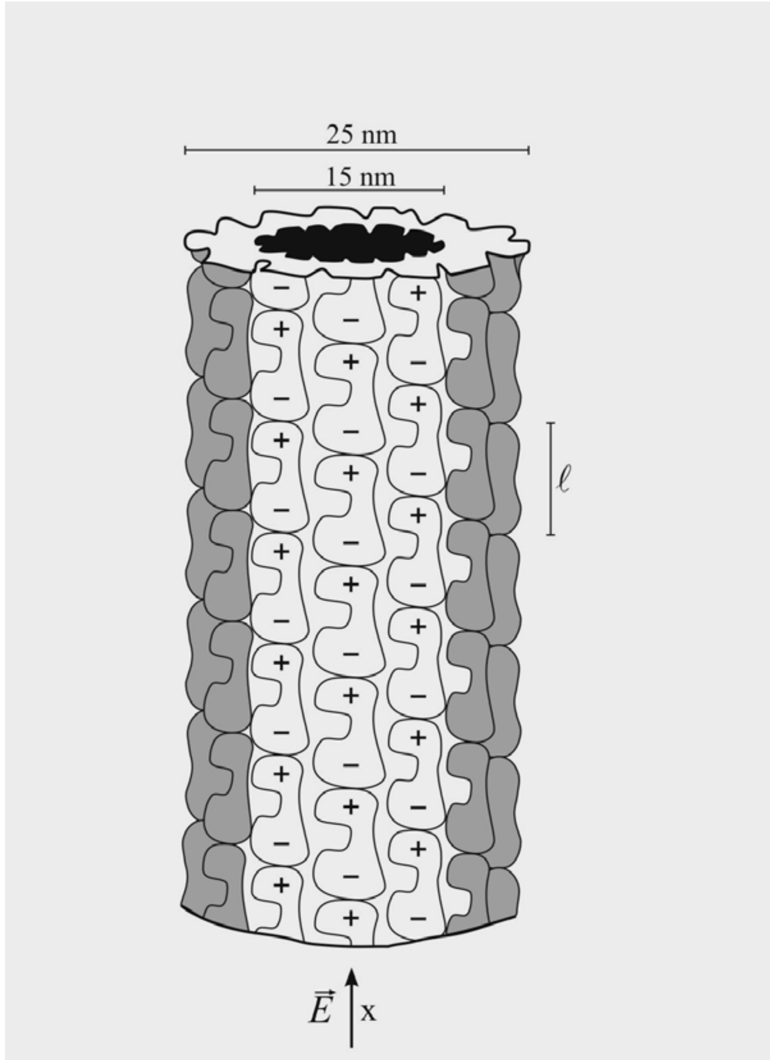
2. Two models

1. Radial (φ - model)
2. Longitudinal (*u* - model)

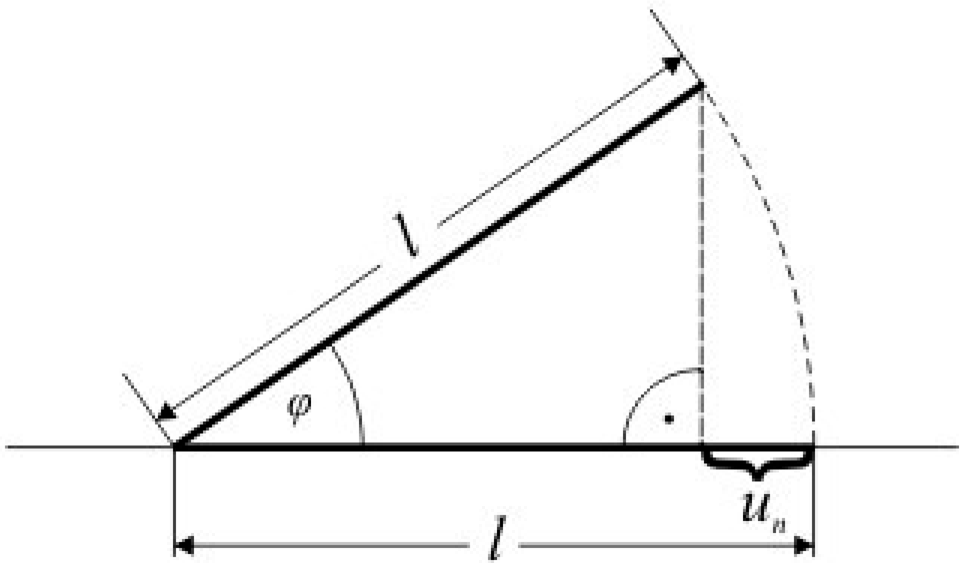
[1] S. Zdravković, M.V. Satarić, A. Maluckov and A. Balaž, Submitted to *Eur. Phys. J. E*

[2] S. Zdravković, L. Kavitha, M. V. Satarić, S. Zeković, J. Petrović, *Chaos, Solitons Fract.* **45** (2012) 1378

Approximation: One degree of freedom per dimer


25 nm
15 nm
ℓ
$\vec{E}$
x

Longitudinal degree of freedom



Real longitudinal model (z-model):

[3] S. Zdravković, M.V. Satarić and S. Zeković, *Europhys. Lett.* **102** (2013) 38002

Procedure

1. Hamiltonian
2. Hamilton equations

Dynamical equations of motion

3.a Continuum approximation
3.b Semi-discrete approximation

3.a Partial differential equation
Ordinary differential equation
3.b Nonlinear Schrödinger equation

φ - model:

$$H = \sum_n \left[\frac{I}{2}\dot{\varphi}_n{}^2 + \frac{k}{2}\left(\varphi_{n+1} - \varphi_n\right)^2 - pE\cos\varphi_n \right]$$

$$H = \sum_n \left[\frac{I}{2}\dot{\varphi}_n{}^2 + \frac{k}{2}\left(\varphi_{n+1} - \varphi_n\right)^2 - pE + pE\left(\frac{\varphi_n{}^2}{2} - \frac{\varphi_n{}^4}{24} \right) \right]$$

U - model:

$$H = \sum_n \left[\frac{m}{2}\dot{u}_n{}^2 + \frac{k}{2}\left(u_{n+1} - u_n\right)^2 + V(u_n) \right]$$

$$V(u_n) = -qEu_n - \frac{1}{2}Au_n^2 + \frac{1}{4}Bu_n^4$$

φ - model:

$$H = \sum_n \left[\frac{I}{2} \dot{\varphi}_n^{\ 2} + \frac{k}{2} \left(\varphi_{n+1} - \varphi_n \right)^2 - pE + pE \left(\frac{\varphi_n^{\ 2}}{2} - \frac{\varphi_n^{\ 4}}{24} \right) \right]$$

$$\varphi = \psi \sqrt{6}$$

U - model:

$$V(u_n) = -Cu_n - \frac{1}{2} Au_n^2 + \frac{1}{4} Bu_n^4$$

$$u = \sqrt{\frac{A}{B}} \psi$$

Dynamical equations of motion

$$I\ddot{\varphi}_n - k\left(\varphi_{n+1} + \varphi_{n-1} - 2\varphi_n\right) + pE\sin\varphi_n + \Gamma\dot{\varphi}_n = 0$$

$$m\ddot{u}_n - k\left(u_{n+1} + u_{n-1} - 2u_n\right) - qE - Au_n + Bu_n{}^3 + \gamma\dot{u}_n = 0$$

$$\frac{I}{pE}\ddot{\psi}_n - \frac{k}{pE}\left(\psi_{n+1} + \psi_{n-1} - 2\psi_n\right) + \psi_n - \psi_n{}^3 + \frac{\Gamma}{pE}\dot{\psi}_n = 0$$

$$\frac{m}{A}\ddot{\psi}_n - \frac{k}{A}\left(\psi_{n+1} + \psi_{n-1} - 2\psi_n\right) - \psi_n + \psi_n{}^3 + \frac{\gamma}{A}\dot{\psi}_n - \sigma = 0$$

3. Two approximations

3.a) Continuum approximation

$$\frac{I}{pE}\ddot{\psi}_n - \frac{k}{pE}\left(\psi_{n+1} + \psi_{n-1} - 2\psi_n\right) + \psi_n - \psi_n^{\ 3} + \frac{\Gamma}{pE}\dot{\psi}_n = 0$$

PDE $\Rightarrow$ **ODE**

Traveling wave ansatz:

$$\xi = \kappa(x - vt) \qquad \Rightarrow \qquad \psi = \psi(x,t) = \psi(\xi)$$

φ - model:

$$\alpha \frac{d^2\psi}{d\xi^2} - \rho \frac{d\psi}{d\xi} + \psi - \psi^3 = 0$$

$$\alpha = \frac{I\omega^2 - kl^2\kappa^2}{pE} \qquad \rho = \frac{\omega\Gamma}{pE}$$

U - model:

.

$$\alpha \frac{d^2\psi}{d\xi^2} - \rho \frac{d\psi}{d\xi} - \psi + \psi^3 - \sigma = 0$$

$$\alpha = \frac{m\omega^2 - kl^2\kappa^2}{A} \qquad \rho = \frac{\gamma\omega}{A} \qquad \sigma = \frac{qE}{A\sqrt{A/B}}$$

Solutions of equation $$\alpha \frac{d^2\psi}{d\xi^2} - \rho \frac{d\psi}{d\xi} - \psi + \psi^3 - \sigma = 0$$

4 procedures

P.1. Standard procedure
P.2. Modified extended tangent hyperbolic function method
P.3. Jacobian elliptic functions
P.4. Factorization method

Review paper:

[4] S. Zdravković and M. Đekić, Mathematical Methods in Nonlinear Dynamics of Microtubules. Submitted to *Sci. World J.*

P.1. Standard procedure

[5] A. Gordon, *Physica* **146** B (1987) 373
[6] M. V. Satarić, J. A. Tuszyński and R. B. Žakula, *Phys. Rev. E* **48** (1993) 589

P.2. Modified extended tangent hyperbolic function method

[7] A. H. A. Ali, *Phys. Lett. A* **363** (2007) 420
[8] S. Zdravković, L. Kavitha, M. V. Satarić, S. Zeković and J. Petrović, *Chaos Solitons Fract.* **45** (2012) 1378

P.3. Jacobian elliptic functions

[9] S. Zeković, S. Zdravković, L. Kavitha and A. Muniyappan, To be published in *Chin. Phys. B*.

P.4. Factorization method

[10] S. Zdravković, S. Maluckov, M. Đekić, S. Kuzmanović and M. V. Satarić, Submitted to *Nonlinearity*

P.2. Modified extended tangent hyperbolic function method

$$\alpha \frac{d^2\psi}{d\xi^2} - \rho \frac{d\psi}{d\xi} - \psi + \psi^3 - \sigma = 0$$

$$\psi = a_0 + \sum_{i=1}^{M} \left(a_i \Phi^i + b_i \Phi^{-i} \right)$$

$$\Phi = \propto \tanh\left(C\xi \right)$$ tangent hyperbolic function method

$$\frac{d\Phi}{d\xi} = b + \Phi^2$$ extended tangent hyperbolic function method

$$\psi = a_0 + \sum_{i=1}^{M} \left(a_i \Phi^i + b_i \Phi^{-i} \right)$$

$$\frac{d\Phi}{d\xi} = b + \Phi^2$$ Riccati

a) $b > 0$ $\Phi = \sqrt{b}\tan\left(\sqrt{b}\,\xi\right)$ or $\Phi = -\sqrt{b}\cot\left(\sqrt{b}\,\xi\right)$

b) $b = 0$ $\Phi = -\dfrac{1}{\xi}$

c) $b < 0$ $\Phi = -\sqrt{-b}\tanh\left(\sqrt{-b}\,\xi\right)$ or

$$\Phi = -\sqrt{-b}\coth\left(\sqrt{-b}\,\xi\right)$$

$$\alpha \frac{d^2\psi}{d\xi^2} - \rho \frac{d\psi}{d\xi} - \psi + \psi^3 - \sigma = 0$$

$$\psi = a_0 + \sum_{i=1}^{M} \left(a_i \Phi^i + b_i \Phi^{-i} \right)$$

$$M = 1$$

$$\psi = a_0 + a_1 \Phi \qquad \Phi = -\sqrt{-b}\tanh\left(\sqrt{-b}\,\xi\right)$$

Unknown parameters: a_0, a_1, b, α

$$\left.\begin{aligned}
&-2a_0 + 8a_0^{\ 3} + \sigma = 0 \\
&\rho = 3a_0 a_1 \\
&2\alpha = -a_1^{\ 2} \\
&-1 + 3a_0^{\ 2} + 2\alpha b = 0
\end{aligned}\right\}$$

$$\alpha < 0 \qquad\qquad b = \frac{3a_0^{\ 2} - 1}{a_1^{\ 2}}$$

[11] V. Smirnov, Kurs vishey matematiki, tom 1, Nauka, Moscow 1965. (In Russian).

$$a_{01} = \frac{1}{2\sqrt{3}}\left(\cos F + \sqrt{3}\sin F\right)$$

$$a_{03} = -\frac{1}{\sqrt{3}}\cos F$$

$$a_{02} = \frac{1}{2\sqrt{3}}\left(\cos F - \sqrt{3}\sin F\right)$$

$$F = \frac{1}{3}\arccos\left(\frac{\sigma}{\sigma_0}\right)$$

$$\sigma_0 = \frac{2}{3\sqrt{3}}$$

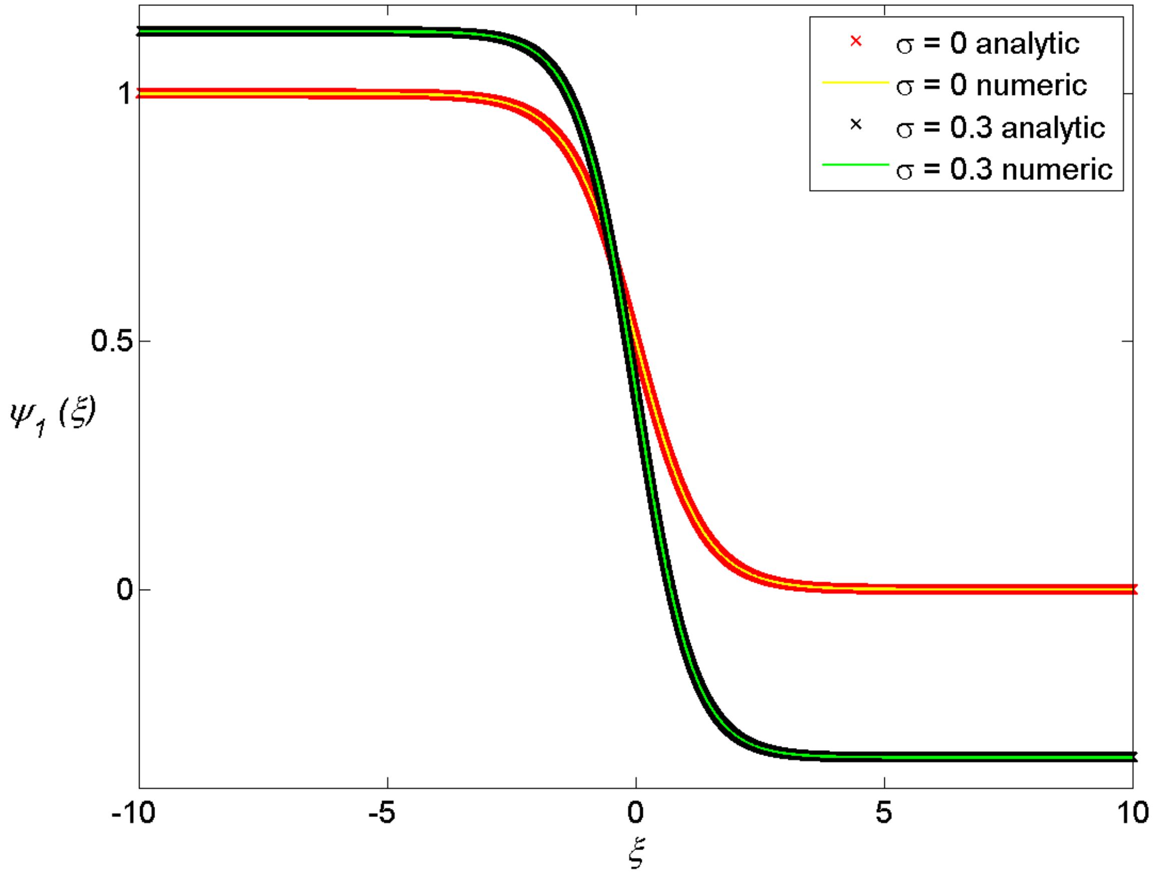
$$b = \frac{3a_0^{\ 2} - 1}{a_1^{\ 2}}$$

$$\sigma < \sigma_0 \qquad \Rightarrow \qquad b < 0$$

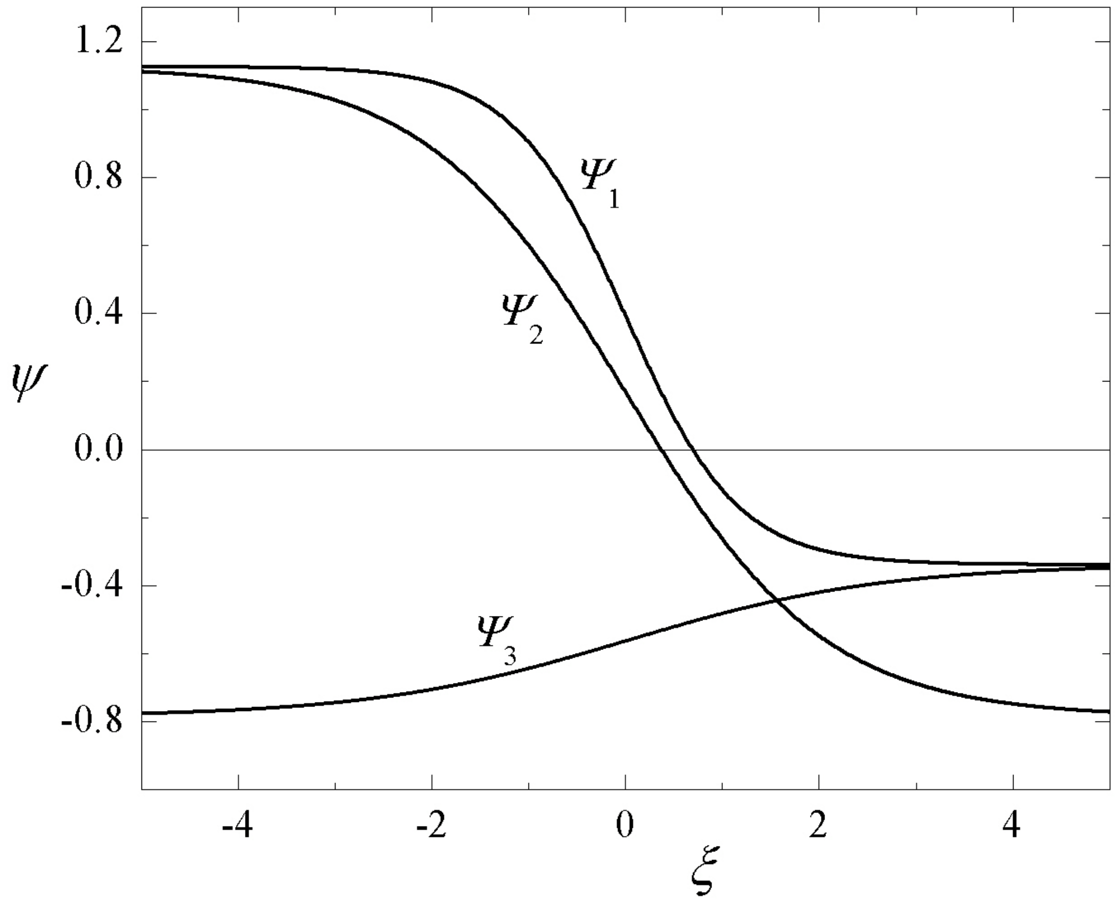
$$\psi = a_0 + a_1 \Phi \qquad \Phi = -\sqrt{-b}\tanh\left(\sqrt{-b}\,\xi\right)$$

$$b = \frac{3a_0^{\ 2} - 1}{a_1^{\ 2}}$$

$$\psi_i(\xi) = a_{0i} - \sqrt{1 - 3a_{0i}^{\ 2}}\tanh\left(\frac{3a_{0i}}{\rho}\sqrt{1 - 3a_{0i}^{\ 2}}\,\xi\right)$$


σ = 0 analytic
σ = 0 numeric
σ = 0.3 analytic
σ = 0.3 numeric
1
0.5
0
ψ1 (ξ)
-10
-5
0
5
10
ξ

$$\rho = 1$$



$\rho = 1$

$\sigma = 0.3$

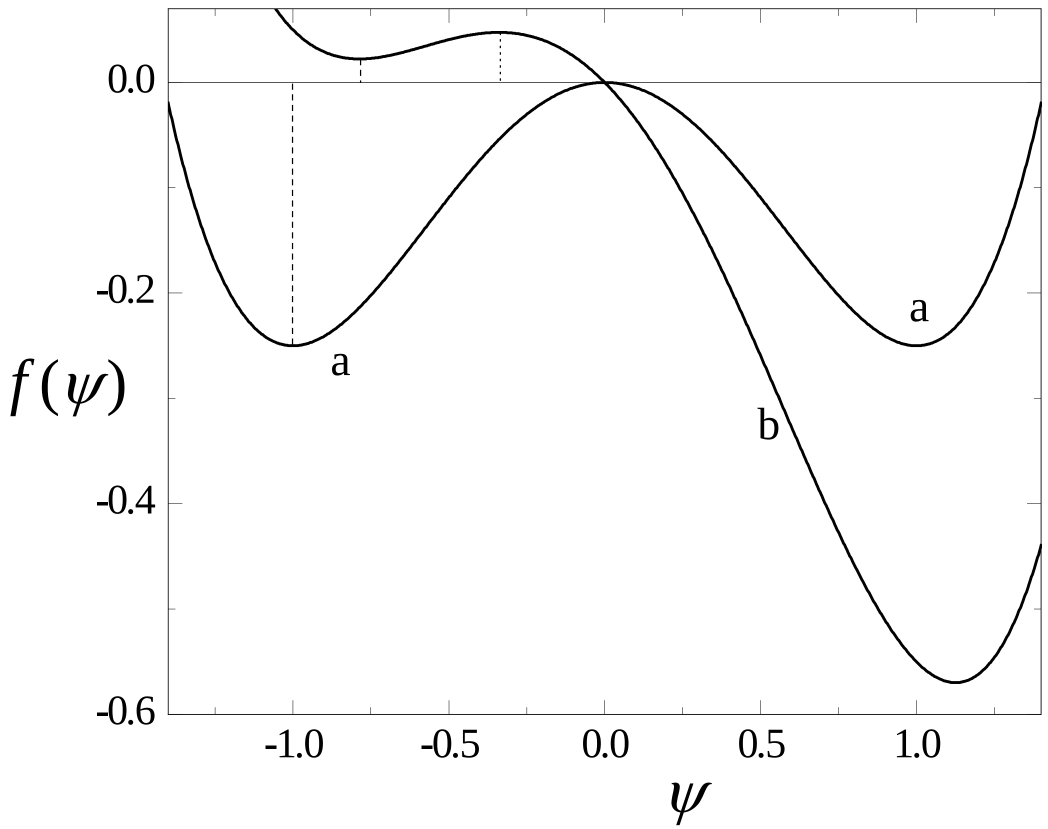
Physical meaning?

$$H = \sum_n \left[\frac{m}{2} \dot{u}_n^{\,2} + \frac{k}{2}\left(u_{n+1} - u_n\right)^2 + V(u_n) \right]$$

$$V(u_n) = -\frac{1}{2} A u_n^2 + \frac{1}{4} B u_n^4 - qEu_n$$

$$V(\psi) = \frac{A^2}{B} f(\psi)$$

$$f(\psi) = -\sigma\psi - \frac{1}{2}\psi^2 + \frac{1}{4}\psi^4$$



(a) $\sigma = 0$ ψ_{R} ψ_{M} ψ_{L}

(b) $\sigma = 0.3$

$$\psi_1(-\infty) = \psi_{\mathrm{R}} \qquad \psi_1(+\infty) = \psi_{\mathrm{max}}$$

$$\psi_2(-\infty) = \psi_{\mathrm{R}} \qquad \psi_2(+\infty) = \psi_{\mathrm{L}}$$

$$\psi_3(-\infty) = \psi_{\mathrm{L}} \qquad \psi_3(+\infty) = \psi_{\mathrm{max}}$$

$$\psi_1: \quad R \rightarrow \mathrm{max}$$

$$\psi_2: \quad R \rightarrow L$$

$$\psi_3: \quad L \rightarrow \mathrm{max}$$

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3. Two approximations

3.a) Continuum approximation

$$\frac{I}{pE}\ddot{\psi}_n - \frac{k}{pE}\left(\psi_{n+1} + \psi_{n-1} - 2\psi_n\right) + \psi_n - \psi_n{}^3 + \frac{\Gamma}{pE}\dot{\psi}_n = 0$$

PDE $\Rightarrow$ **ODE**

3.b) Semi-discrete approximation

$$\frac{I}{pE}\ddot{\psi}_n - \frac{k}{pE}\left(\psi_{n+1} + \psi_{n-1} - 2\psi_n\right) + \psi_n - \psi_n^{\ 3} + \frac{\Gamma}{pE}\dot{\psi}_n = 0$$

[12] M. Remoissenet, *Phys. Rev. B* **33** (1986) 2386

[13] R.K. Dodd, J.C. Eilbeck, J.D. Gibbon and H.C. Morris, "*Solitons and Nonlinear Wave Equations*", Academic Press, Inc., London 1982

[14] T. Kawahara, *J. Phys. Soc. Japan* **35** (1973) 1537

$$\psi_n = \varepsilon \Phi_n \qquad \varepsilon << 1$$

$$\frac{I}{pE}\ddot{\psi}_n - \frac{k}{pE}\left(\psi_{n+1} + \psi_{n-1} - 2\psi_n\right) + \psi_n - \psi_n^{\ 3} + \frac{\Gamma}{pE}\dot{\psi}_n = 0$$

$$\frac{I}{pE}\ddot{\Phi}_n - \frac{k}{pE}(\Phi_{n+1} + \Phi_{n\text{-}1} - 2\Phi_n) + \Phi_n - \varepsilon^2\Phi_n^{\ 3} + O(\varepsilon^3) = 0$$

$$\Phi_n(t) = F(\xi)e^{i\theta_n} + \varepsilon\ F_0(\xi) + \mathrm{cc} + \mathrm{O}(\varepsilon^2)$$

$$\xi = (\varepsilon nl, \varepsilon t) \qquad \theta_n = nql - \omega t \qquad \varepsilon F_2(\xi)\, e^{i2\theta_n}$$

$$nl \to z \qquad Z = \varepsilon z; \qquad T = \varepsilon t$$

$$F(\varepsilon(n \pm 1)l, \varepsilon t) \to F(Z,T) \pm F_Z(Z,T)\varepsilon l + \frac{1}{2}F_{ZZ}(Z,T)\varepsilon^2 l^2$$

$$(\varepsilon^2 F_{TT} - 2i\varepsilon\omega F_T - \omega^2 F)e^{i\theta} + \varepsilon^3 F_{0TT} + \mathrm{cc} =$$

$$= \frac{k}{I}\left\{2F\left[\cos(ql) - 1\right] + 2i\varepsilon l F_Z \sin(ql) + \varepsilon^2 l^2 F_{ZZ}\cos(ql)\right\}e^{i\theta}$$

$$-\frac{pE}{I}\left(F_1 e^{i\theta} + \varepsilon F_0\right)$$

$$+\varepsilon^2 \frac{pE}{I}\left(F^3 e^{i3\theta} + 3\varepsilon F^2 F_0 e^{i2\theta} + 3\varepsilon^2 F F_0^{\,2} e^{i\theta} + 3|F|^2 F e^{i\theta} + 6\varepsilon |F|^2 F_0\right)$$

$e^{i\theta} \qquad \Rightarrow \qquad \omega^2 = \frac{4k\sin^2(ql/2) + pE}{I}$

$$V_g = \frac{lk}{I\omega}\sin(ql)$$

$e^{i0} = 1 \qquad \Rightarrow \qquad F_0 = 0$

$$\Phi_n(t) = F(\xi)e^{i\theta_n} + \varepsilon\, F_0(\xi) + \mathrm{cc} + \mathrm{O}(\varepsilon^2)$$

.

$S \qquad \tau$

$$S = Z - V_g T, \qquad \tau = \varepsilon T$$

$$iF_{\tau} + P\,F_{SS} + Q\,\left|F\right|^2 F = 0$$

$$P = \frac{1}{2\omega}\left[\frac{l^2 k}{I}\cos(ql) - V_g{}^2\right]$$

$$Q = \frac{3pE}{2I\omega}$$

$$F(S,\tau) = A_0\ \mathrm{sech}\left(\frac{S - u_e\tau}{L_e}\right)\exp\frac{iu_e(S - u_c\tau)}{2P}$$

.

$$\psi_n(t) = 2A\mathrm{sech}\left(\frac{nl - V_e t}{L}\right)\cos(\Theta nl - \Omega t)$$

$$A \equiv \varepsilon A_0 = U_e\sqrt{\frac{1-2\eta}{2PQ}}$$

$$L \equiv \frac{L_e}{\varepsilon} = \frac{2P}{U_e\sqrt{1-2\eta}}$$

$$V_e = V_g + U_e$$

$$\Theta = q + \frac{U_e}{2P}$$

$$\Omega = \omega + \frac{(\mathrm{V}_g + \eta U_e)U_e}{2P}$$

$$u_e > 2u_c$$

$$U_e = \varepsilon u_e$$

$$\eta = \frac{u_c}{u_e}$$

Coherent mode

$$V_e = \frac{\Omega}{\Theta}$$

$$\Rightarrow \qquad U_e = \frac{P}{1-\eta}\left[-q + q\sqrt{1 + \frac{2(1-\eta)}{Pq^2}\left(\omega - qV_g\right)}\right]$$

$$0 \le \eta < 0.5$$

,

Viscosity $M_v = -\Gamma\dot{\Phi}_n$ $\beta = \Gamma/2I$

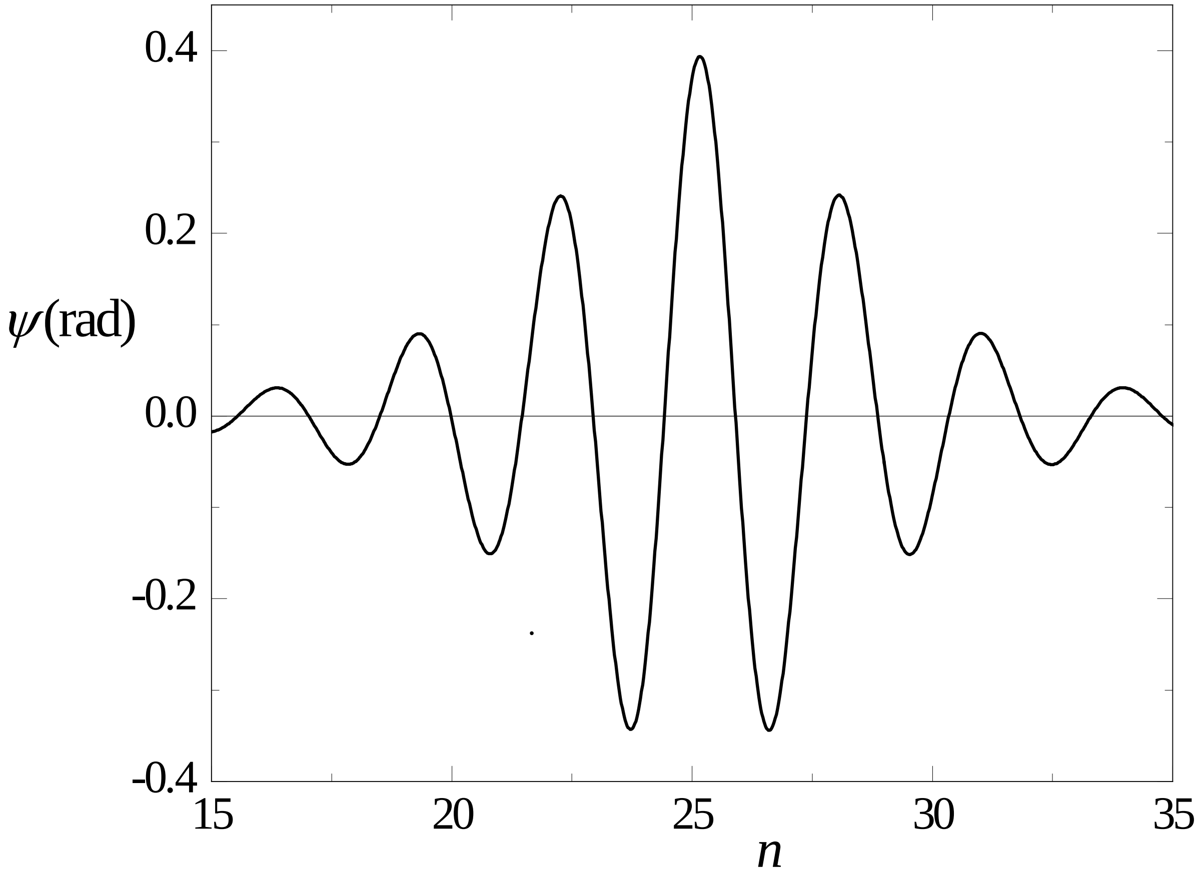
$$NT = \left[-\varepsilon F_T e^{i\theta_\gamma} + i\omega_\gamma F e^{i\theta_\gamma} - \varepsilon^2 F_{0T}\right]\frac{\Gamma}{I} + \mathrm{cc}$$

$$V_\gamma = \frac{\omega V_g}{\sqrt{\omega^2 - \beta^2}}$$

$$iF_\tau + P_\gamma F_{SS} + Q_\gamma \left|F\right|^2 F = 0$$

$$P_\gamma = \frac{1}{2\sqrt{\omega^2 - \beta^2}}\left[\frac{kl^2}{I}\cos(ql) - V_\gamma^{\ 2}\right]$$

$$Q_\gamma = \frac{3pE}{2I\sqrt{\omega^2 - \beta^2}}$$



$t = 3\text{ns}$

$\beta = 0.3\omega$

Localized modulated soliton (breather)

4. Kinks and breathers

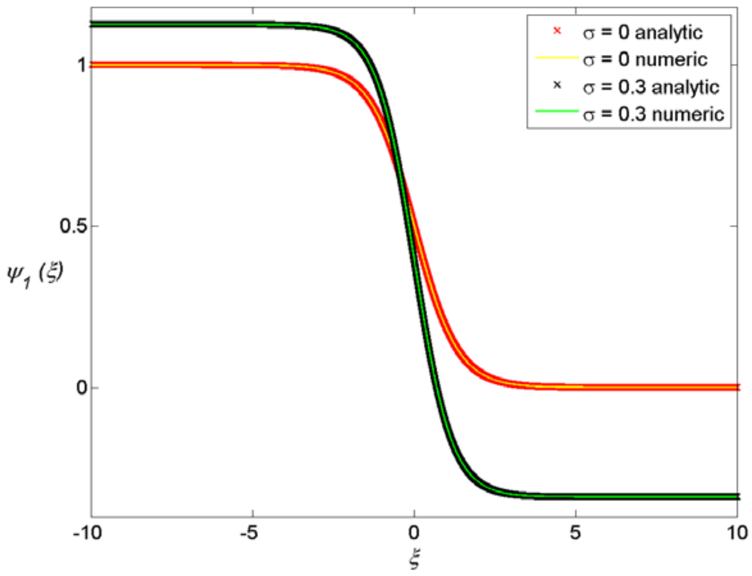
3.a) Continuum approximation

Traveling wave ansatz

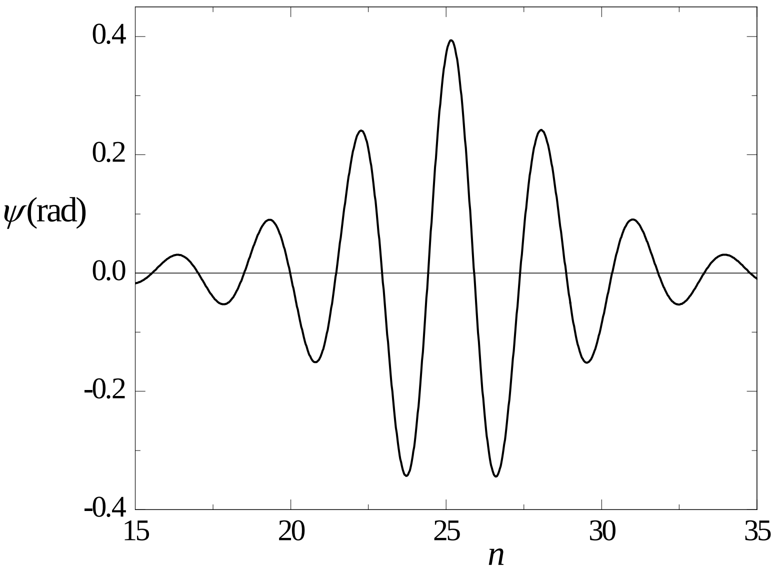
Kink soliton

3.b) Semi-discrete approximation

Localized modulated soliton (breather)



σ = 0 analytic
σ = 0 numeric
σ = 0.3 analytic
σ = 0.3 numeric
1
0.5
0
$\psi_1\ (\xi)$
-10
-5
0
5
10
ξ



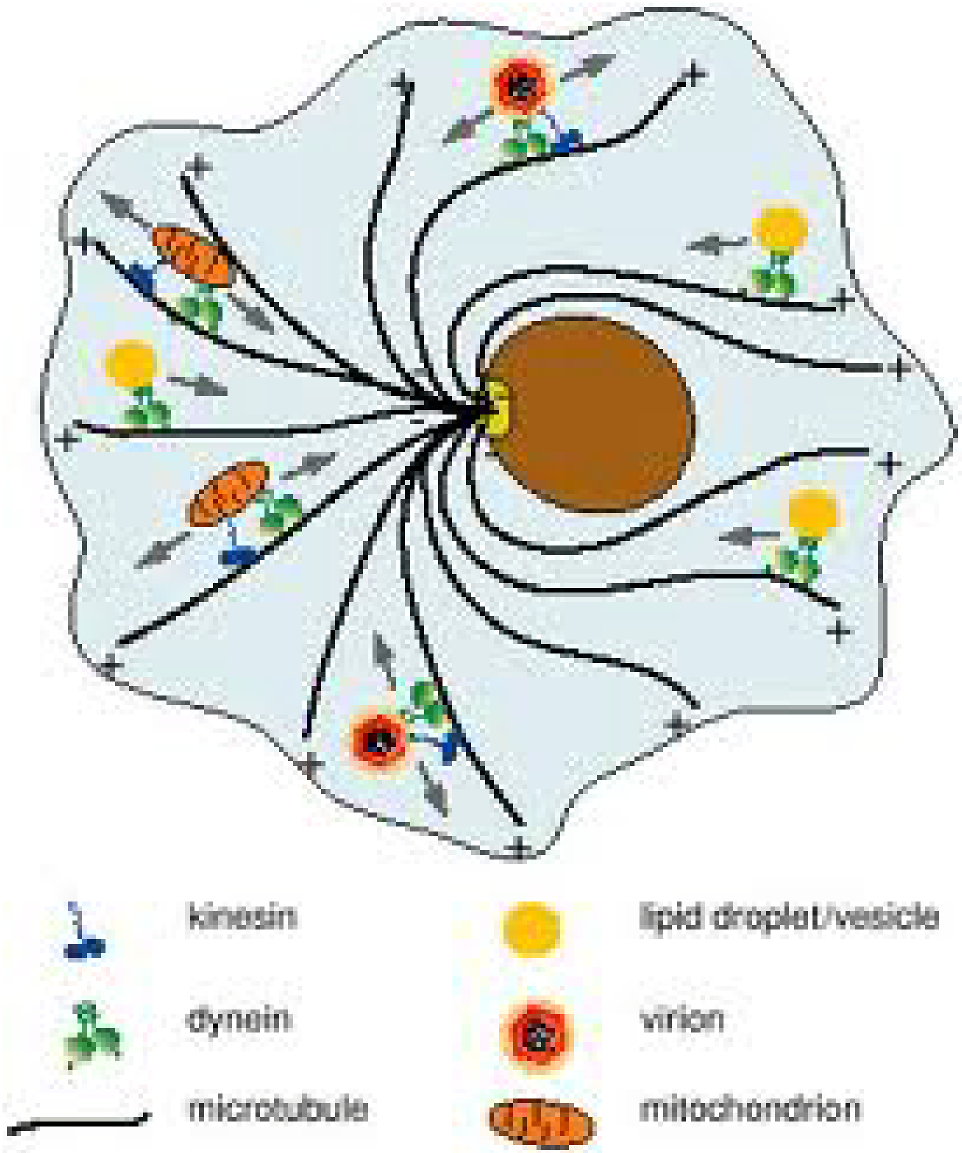
0.4
0.2
0.0
-0.2
-0.4
ψ(rad)
15
20
25
30
35
n

Biological implication 1

Why is a soliton important for a cell?

MTs serve as a “road network” for motor proteins (kinesin and dynein) dragging different “cargos” such as vesicles and mitochondria.

A soliton is a signal which activates a proper motor!


kinesin
dynein
microtubule
lipid droplet/vesicle
virion
mitochondrion

Biological implication 2

$$\varphi(x,t) = \frac{\sqrt{6}}{2}\left[1 + \tanh\left(\frac{3}{4\rho}\xi\right)\right]$$

$$0 < \varphi < \sqrt{6}\ \mathrm{rad}$$

MT begins to crumble.

Maize cob (corn)

MT is dynamically very unstable structure. Its life time in normal cells is about 2-4 hours while its depolymerisation (disintegration) occurs in a few seconds.

Depolymerisation always starts from the biologically positive end, i.e. negatively charged end.

$\varphi(-\infty) = 0$ stable state

$\varphi(+\infty) = \sqrt{6}$ unstable state

Biological equivalence of the instability is the blowups of MT.

5. Further research

1. More general model

φ - model: $$H=\sum_n\left[\frac{I}{2}\dot{\varphi}_n{}^2+\frac{k}{2}(\varphi_{n+1}-\varphi_n)^2-pE\cos\varphi_n\right]$$

U - model: $$H=\sum_n\left[\frac{m}{2}\dot{u}_n{}^2+\frac{k}{2}(u_{n+1}-u_n)^2+V(u_n)\right]$$

$$V(u_n)=-qEu_n-\frac{1}{2}Au_n^2+\frac{1}{4}Bu_n^4$$

More general model

$$H = \sum_n \left[\frac{I}{2}\dot{\varphi}_n{}^2 + \frac{k}{2}\left(\varphi_{n+1} - \varphi_n\right)^2 - pE\cos\varphi_n - \frac{1}{2}A\varphi_n^2 + \frac{1}{4}B\varphi_n^4 \right]$$

2. Kinocilium

Part of acoustic apparatus in vertebrates.

It consists of 9 pairs of parallel MTs.

[15] M.V. Satarić, D.L. Sekulić, B.M. Satarić and S. Zdravković, Localized nonlinear ionic pulses along microtubules tune the mechano-sensitivity of hair cells. Submitted to *Phys. Rev. E*

Thank you for your attention!

* * *

Thanks to organizers of the conference!

* * *

Thanks to Бранко Драговић