External field influence on semiflexible macromolecules: geometric coupling

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Abstract

We suggested a geometric approach to address the external field influence on the DNA molecules, described by the WLC model via geometric coupling. It consists in the introduction of the effective metrics depending on the potential of the external field, with further re-definition of the arc-length parameter and of the extrinsic curvatures of the DNA molecules. It yields the nontrivial impact of the external field in the internal energy of macromolecules. We give the Hamiltonian formulation of this model and perform its preliminary analysis in the redefinition of the initial energy density.

1 Introduction

In recent years, single-molecule techniques have evolved into a powerful toolset for studying the dynamical behavior of many biological processes. It is now possible to follow on the nanometer and millisecond scales the individual trajectory of a single enzyme as it catalyzes a reaction, a molecular motor as it translocates, or a single polypeptide or nucleic acid molecule as it unfolds and refolds [1][2][3].

One of the widely used applications of single-molecule manipulations is the direct investigation of double-stranded DNA (dsDNA). The single-molecule stretching experiments gave a big contribution to the understanding of the dsDNA structure and functionality [4][5][6][7], while the ssDNA or ssRNA are usually described by freely jointed chains with elastic bonds (EFJC) [8].

The WLC Hamiltonian is presented as a functional on a differentiable space curve \( \gamma \) of fixed length \( L \),

\[
E_0^{\text{WLC}} = \frac{l_p k_B T}{2} \int_{\gamma} \kappa_1^2 ds ,
\]

where \( \mathbf{r}(s) \) is the radius vector of an arbitrary point of the curve as a function of the contour distance \( s \) from one end to that point, \( T \) is the temperature, \( k_B \) is the Boltzmann constant, \( l_p \) is the persistence length and \( \kappa_1 \) is the first curvature (rigidity) of the curve, which is defined by the use of the unit vector \( \mathbf{e}_1(s) \), \( \mathbf{e}_1^2 = 1 \) tangential to the curve: \( \kappa_1 = |d\mathbf{e}_1/ ds|, \mathbf{e}_1 = \frac{d\mathbf{r}}{ds} \), where \( s \) is the arc-length of the curve \( \mathbf{r}(\tau) \),

\[
s = \int_{\gamma} |d\mathbf{r}|, \quad ds = \left| \frac{d\mathbf{r}}{d\tau} \right| d\tau
\]

An example of the spatial constraints, imposed on the polymer chain, is the helical structure observed in many biological and synthetic polymers [9]. In order to describe the helical structure of the chain space, following Bugle and Fujita [10] (see also [11]), we need to introduce the unit curvature vector \( \mathbf{e}_2 = \frac{d\mathbf{e}_1/ ds}{|d\mathbf{e}_1/ ds|} \) and define the potential energy of the chain as follows:

\[
E_0^{\text{BF}} = \frac{k_B T}{2} \int_{\gamma} ds \left[ (\kappa_1 - \alpha)^2 + (\kappa_2 - \beta)^2 \right],
\]

where \( \kappa_1 = \mathbf{e}_1 \cdot \mathbf{e}_2 \) is a first curvature (rigidity) of \( \gamma \) and \( \kappa_2 = \sqrt{|d\mathbf{e}_2/ ds|^2 - \kappa_1^2} \) is a second curvature (torsion) of the curve \( \gamma \). The \( \alpha \) and \( \beta \) parameters are supposed to be the equilibrium bending and torsion constants. The absolute minimum of the potential energy is given by \( \kappa_1 = \alpha \) and \( \kappa_2 = \beta \) and corresponds to the regular helix with radius \( r_0 = \frac{\alpha}{\sqrt{\alpha^2 + \beta^2}} \) and pitch \( h = \frac{2\pi |\beta|}{\alpha^2 + \beta^2} \).

In this respect the paper by Feoli, Nesterenko and Scarpetta [12] deserves to be mentioned. There the authors suggested to describe the DNA molecules by the functional

\[
E_0 = \int_{\gamma} (c_0 + c_1 \kappa_1) ds ,
\]
whose minimum corresponds to the helical configuration of the curve. Unfortunately, these authors interpreted the functional \( E_0 \) as a free energy of the DNA molecules, which yields some inconsistencies in the interpretation of the results. The importance of that paper is not only in the suggestion to describe the DNA molecules by the functionals linear on the curvature, but to operate with the functionals depending on extrinsic curvatures by the use of the Dirac’s theory of constrained systems \[13\]. Further below, we will discuss this issue in more detail.

It is not occasional, that in all listed models the energy of the macromolecule is defined by the use of extrinsic curvatures of the macromolecule curve. Indeed, the (linear) density of the energy of the macromolecule should \textit{a priori} depend on the geometric characteristic of the curves and be independent on the way of their description. Hence, it should depend on the functions of the curve \( \gamma \) which are invariant under its motions (rotations and translations), i.e. on its extrinsic curvatures \( \kappa_I \), \( 0 < I \leq D - 1 \) (where \( D \) is the dimensionality of the space) \[14\].

From this viewpoint the common approach, for taking into account the external field influence, seems to be ill-defined. It consists in the naive adding to the energy functional given further below in \( E_0 \) of the potential energy term \[15\]

\[
E = E_0 + \int_\gamma V(r) ds, \tag{1.5}
\]

where \( V(r(s)) \) is the potential of the external field.

The geometric (“macroscopic”) inconsistency is that the energy functional of the macromolecule becomes the function of a quantity, which is not invariant under the motions of the curve (rotations and translation in Euclidean space).

The physical (“microscopic”) inconsistency of this approach is the independence of the chain flexibility (e.g. the persistence length \( l_p \)) on the external field. While the stretching or the compressing fields substantially restricted the set of available conformations of each repeated unit of the polymeric chain. Thus, a strong enough external field should affect the chain flexibility, and the persistence length \( l_p \). This issue should be relevant, e.g. for the confinement-induced changes of the persistence length observed in \[16\]. The effective compressing field, describing the intra - chain attraction and chain confinement in restricted geometries yields a substantial change of the apparent persistence length \[17, 18\].

The purpose of the present paper is to suggest an alternative way for taking into account the external field influence, which seems to be free from the above discrepancies. Namely, we suggest to involve the external field in the definition of the line element \( ds \), associating it with the effective metric

\[
g_{AB} = (1 + V(r))^2 \delta_{AB} \equiv n^2(r)\delta_{AB}, \tag{1.6}
\]

and to define the extrinsic curvatures \( \kappa_I \), in accordance with Frenet equations, on the space equipped with this effective metric.

Hence, we suggest to preserve the functional dependence of the energy density from the extrinsic curvature, but modify the definition of the arc-length, and consequently, of the extrinsic curvatures.

The paper is organized as follows.

In the Second section we present the explicit expression of the suggested geometric model of the macromolecule interaction with the external field, and discuss the analogies of this model with relativistic particle systems and with geometric optics.

In the Third section we give its Hamiltonian formulation and analyze it in the framework of the Dirac’s theory of constrained systems.

2 The model

We suggest to describe the external field influence on the macromolecule by the energy functional

\[
E_0 = \int_\gamma F(\kappa_1, ..., \kappa_N) d\tilde{s}, \tag{2.1}
\]

where

- \( F(\kappa_I) \) is the energy density in the initial (noninteracting) DNA model. It can be chosen say, as in \[14\], \[13\], \[14\].

\[2\]
The element of arclength (or control length) \( ds \) is defined in accordance with the metric (1.6),
\[
    ds = n(\mathbf{r})|\mathbf{r}|d\tau \equiv \hat{s}d\tau,
\]
where \( \tau \) is an arbitrary parameter defining the curve \( \gamma; \mathbf{r} = \mathbf{r}(\tau) \).

The extrinsic curvatures \( \kappa_I \) are defined, via Frenet equations, on the space equipped by the effective metric (1.6),
\[
    \frac{dr}{\hat{s}d\tau} = e_1, \quad \frac{De_a}{\hat{s}d\tau} = \kappa_a e_{a+1} - \kappa_{a-1} e_{a-1},
\]
Here
\[
    D = \frac{d}{d\tau} + \hat{\Gamma}(\mathbf{r}), \quad (\hat{\Gamma})_B^A = \Gamma_{BC}^A \hat{e}^C, \quad e_a \cdot e_b = \delta_{ab}, \quad e_0 = e_{D+1} = 0, \quad I = 1, \ldots, D
\]
with \( e_0, e_j \equiv e^{(i)} e^{(j)} g_{AB} e^{(i)} e^{(j)} \), being \( D \) the dimensionality of the space and \( \Gamma_{BC}^A \) the Christoffel symbols of the effective metric
\[
    \Gamma_{AB} = n_A \delta_{CB} + n_B \delta_{CA} - n_C \delta_{AB}, \quad n_A \equiv \partial_A \log n.
\]
Similarly to the Euclidean case, the curvatures \( \kappa_1, \ldots, \kappa_{D-1} \) are positive functions, and the highest curvature (torsion), \( \kappa_{D-1} \) can take both positive and negative values. If some \( \kappa_I \neq 0 \), then \( \kappa_1 \neq 0 \). Vice versa, from \( \kappa_I = 0 \), it follows that \( \kappa_1 = 0 \). The price for the geometrization of the model is the further mathematical complication of the system. In spite of the apparent simplicity, the analysis of models with the energy functional (2.1) is not a simple task: the matter is that the energy density \( F \) in (2.1) depends on higher derivatives and should be analyzed in the framework of the Dirac’s theory of constrained systems [13]. Fortunately, in the eighties such functionals were widely studied in the context of the (relativistic) spinning particles. Namely, the functionals (2.1) in the Minkowski spacetime, with \( s \) being a world-line parameter were considered. These studies were inspired by the papers Polyakov devoted to the Chern-Simons theories and rigid strings [20]. Various systems depending on the first and the second curvatures of the path in three- and four- dimensional Minkowski spaces were studied in details, mostly by Plyushchay (see [21, 22] and references therein). By this reason the relevant formalism for analyzing such systems on the base of the Frenet equations has been developed by one of the authors [23]. Almost all systems depending on extrinsic curvatures either by isospin (i.e. by internal degrees of freedom), or spin (in the case when they are proportional to a single curvature, see [22, 24]). In the context of macromolecules it means, that the systems with energy density depending on extrinsic curvatures of macromolecules should have internal degrees of freedom. Now, any macromolecule is a sequence of atoms connected by chemical bonds. That is why, the
universal way of any change of chain conformation is the change of dihedral angles, caused by rotation around the chemical bonds. Thus, any polymeric chain has its internal rotational degrees of freedom, which should be obviously identified with the isospin of the system. These studies were performed on flat spaces, mostly. The only exceptions are, seemingly \[25\] [24]. A qualitative observation there is that, for Lagrangians (in our case: energy densities) with linear dependence on extrinsic curvatures, the introduction of non-Euclidean metrics drastically changes the properties of the system, including the dimensionality of the internal space. Only for the constant curvature spaces (e.g. spheres, hyperboloids) non-Euclidean metrics do not change essentially the properties of such systems. In three-dimensional space, in our notation it corresponds to the choice

\[ n(r) = a_0/(1 + \beta r^2) \]

(2.7)
corresponding to the three-dimensional sphere or hyperboloid (depending on the choice of the sign of \( \beta \)).

The suggested DNA model has an obvious analogy with the geometric optic, where the trajectory of light in the media with refraction index \( n(r) \) corresponds to the minimum of the functional (under assumption that the helicity of light is neglected)

\[ S_{Fermat} = \int ds, \quad ds = n(r)|\dot{r}|d\tau. \]

(2.8)

Hence, the generic action \([2.1]\) defined on such “effectively” curved space, will take into account the interaction of the spin (helicity) of the light with the media, i.e. the phenomenon of the “optical Hall effect”, consisting in the deviation of the light trajectory from that given by Fermat Principle, due to the feedback from the polarization \[26\]. Let us also mention, in this respect, the recent paper \[27\], where the analysis of the model \([1.4]\) with a non-constant effective metric has been performed in some details, in the context of geometric optic.

So, we suggest to describe the DNA molecules interacting with the external field by the functional \(2.1\), where the arc-length is defined by the expression \( \tilde{s} \equiv (1 + V(r))|\dot{r}|d\tau \), and the extrinsic curvatures \( \kappa_1, \ldots, \kappa_N, N < D \) are defined in accordance with modified Frenet equations \(2.3\).

### 3 Hamiltonian formulation

It is seen from the Frenet equations \(2.3\), that the \(I\)-th extrinsic curvature \( \kappa_I \) depends on the \((I+1)\)-th derivative, \( \kappa_I = \kappa_I(r^{(i)}) \), so that the energy density \( F(\kappa_i) \) in \(2.1\) depends on the \((N+1)\)-th derivative. By this reason the study of its Euler-Lagrange equations is not a simple task. To simplify the analysis of \(2.1\), let us consider the variationally equivalent functional, whose integrand depends on the first derivatives only (see \(23, 24, 28\) for further details).

Precisely, we replace the initial energy density \( \mathcal{L} \) by the following variationally equivalent one:

\[ \tilde{F} = F(\kappa_1, \ldots, \kappa_N) - \lambda \left( \kappa_N - \sqrt{\frac{\sum_{i=1}^{D} e_i}{\tilde{s} \dot{r}}}^2 - \kappa_N^2 \right) + p \left( \frac{dx}{\tilde{s} \dot{r}} - e_1 \right) + \sum_{i=1}^{D} p_{i-1} \left( \frac{De_{i-1}}{\tilde{s} \dot{r}} - \kappa_{i-1} e_i + \kappa_{i-2} e_{i-2} \right) - \sum_{i,j} d^{ij} (e_i e_j - \delta_{ij}) \]

(3.1)

where \( \tilde{s}, \kappa_{i-1}, d^{ij}, p_{i-1}, e_i, \lambda \) play the role of independent variables, and the relation

\[ \kappa_N^2 = \left( \frac{De_N}{\tilde{s} \dot{r}} \right)^2 - \kappa_N^{-2} \]

which follows from \(2.3\) is taken into account. Here and further below, we use the following notation for the scalar products: \( p_i \cdot p_j \equiv p_{(i)A} g_{AB} p_{(j)B} \), \( p_i \cdot e_j \equiv p_{(i)A} e_{jA} \), where, upon summation the indices \( A, B \) take the values \(1, \ldots, D\), and \( i, j = 1, \ldots, N \).

It is easy to see, that varying the energy density \( \tilde{F} \) by \( \kappa_N \), we shall get \( \lambda = \partial F/\partial \kappa_N \), while its variations by \( p, p_{i-1} \) and \( d_{ij} \) will yield the Frenet equations restoring the dependence of \( \kappa_i \) on \( r^{(i)} \).

The Hamiltonian formulation of the system with the singular “Lagrangian” \(3.1\) on the Euclidean space was carried out in \(23\). Its extension to curved space is straightforward. For the “Lagrangians” linear on extrinsic
curvatures it was considered in [24], and for the generic case in [28]. In accordance with this paper, the Euler-Lagrange equations of the functional with the energy density \( \tilde{F} \) are given by the constrained Hamiltonian system,

\[
\omega = dp \land dr + \sum_{i=1}^{N} dp_i \land de_i, \quad H = h_0 + \sum_{i} \kappa_i \phi_i + \sum_{i,j} d^{ij}(e_i e_j - \delta_{ij}),
\]

(3.2)

with the following set of constraints (including some gauge fixing conditions, see for details [28, 28]):

\[
\phi_0 \equiv \pi e_1 + \sum_i \kappa_i F, i = F \approx 0, \quad \text{where } \pi \equiv p - \Gamma, \quad \Gamma_A \equiv \sum_{i=1}^{N} \Gamma^C_{ABP(0)C} e_i^B
\]

(3.3)

\[
p_i e_j \approx 0, \quad i \geq j
\]

(3.4)

\[
e_i e_j - \delta_{ij} \approx 0,
\]

(3.5)

\[
\phi_{i-1} \equiv p_{i-1} e_i - p_i e_{i-1} - F_{i-1} \approx 0, \quad 2\phi_N = \frac{1}{F_N} \left( p_N p_N - \sum_i (p_N e_i)(p_N e_i) \right) - F_N \approx 0
\]

(3.6)

For \( \det \partial^2 F/\partial \kappa_i \partial \kappa_j \neq 0 \), we can resolve the equations (3.6), expressing \( \kappa_i \) via \( p_i, e_j \). After that we should substitute these expressions for \( \kappa_i \) in (3.3).

Otherwise, for \( \text{corank } \partial^2 F/\partial \kappa_i \partial \kappa_j = M \neq 0 \), we can resolve only \( (N-M) \) equations in (3.6), while the rest will appear as a primary constraint, with the \( M \) undefined functions on \( \kappa_i \) playing the role of Lagrangian multipliers.

After these manipulations we will get the constrained Hamiltonian system with \( N(N-1)+1 \) primary constraints given by (3.3)–(3.5) and with \( M \) primary constraints obtained from (3.6). Then, we should perform the Dirac’s procedure of “stabilization” of the above set of constraints, i.e. require \( \{ \ldots , H \} \approx 0 \), where by ... we enclosed the set of primary constraints. This requirement will either fix the values of Lagrangian multipliers, or yield an additional set of “secondary” constraints. Then, stabilizing the obtained set of secondary constraints, we shall either get the new set of secondary constraints, or will further fix the values of Lagrangian multipliers, and so on (see, e.g., [13]).

It is easy to observe, that the “stabilization” of the constraints (3.4) fixes the values of the Lagrangian multipliers \( d^{ij} \), while the stabilization of the remaining set depends on the concrete properties of the function \( F(\kappa_1, \ldots, \kappa_N) \).

For example, for the energy densities with a non-degenerate quadratic dependence on curvatures, \( F = c_{ij} \kappa_i \kappa_j \), \( \det c_{ij} \neq 0 \), which involves, as a particular case, the WLC model (1.1) and Buggle-Fujita model (1.3), there are no secondary constraints. The whole set of (primary) constraints is divided in the second-class constraints given by (3.3), (3.5), and the single first-class constraint given by (3.3). As a consequence, we get that the dimensionality of the physical phase space is \( 2D(N+1) - 2 - N(N-1) = 2DN - N(N-1) \). In contrast with this case, in the systems with linear energy densities, \( F = c_1 \kappa_i + c_0 \), the whole set of constraints and their algebra, essentially depend on the values of the constants \( c_i \) and on the properties of the effective metric (1.6).

Hence, in contrast with the functionals with linear dependence on curvature, in the case of quadratic dependence, the introduction of the curved metric does not essentially change the structure of the phase space of the system, being reflected only on the functional dependence of the Hamiltonian from the external field.

To complete this general consideration, let us present the following useful expressions, which should be useful for the further analysis of the systems under consideration.

At first, let us write down the non-zero Poisson brackets between the functions \( \pi e_i, \pi p_i, \pi^2 \):

\[
\{\pi e_i, \pi e_j\} = \mathcal{R}(e_i, e_j), \quad \{\pi p_i, \pi p_j\} = \mathcal{R}(p_i, p_j)
\]

(3.7)

\[
\{\pi e_i, \pi p_j\} = \mathcal{R}(e_i, p_j) - \pi^2 \delta_{ij}, \quad \{\pi e_i, \pi^2\} = -2\mathcal{R}(\pi, e_i), \quad \{\pi p_i, \pi^2\} = -2\mathcal{R}(\pi, p_i)
\]

where

\[
\mathcal{R}(a, b) \equiv \sum_{i=1}^{N} R(p_i|e_i, a, b).
\]

(3.8)

is the Riemann tensor associated with the effective metric (1.6).

Then, let us present the expression for the Riemann tensor in the three-dimensional space, where it is uniquely expressed via the Ricci tensor

\[
R_{ABCD} = R_{(2)ACBD} - R_{(2)ADB|C} + R_{(2)BDAGC} - R_{(2)BC|AGD} + \frac{R_0}{2} (g_{ADG}g_{BC} - g_{AC}g_{BD}),
\]

(3.9)
where $R_2$ is the Ricci tensor and $R_0$ is the scalar curvature of the space. For the conformal flat metric \((1.6)\) the Ricci tensor is defined by the formulae

$$R_{AC} = -g_{AC}(n_{DD} + 3n_D^2) - n_{A,C} + n_{A}n_{C}, \quad n_A \equiv \partial_A \log n. \quad (3.10)$$

All considerations above were quite general, with a generic functional dependence of the energy density on the extrinsic curvatures, and they have been formulated in the $D$-dimensional space. As an example, let us give the explicit formulation of the WLC model \((1.1)\), with the additional constant term $c_0$

$$F = \frac{c}{2} \kappa_1^2 + c_0. \quad (3.11)$$

In this case the Hamiltonian system \((3.2)\) reads

$$\omega = dp \wedge dr + dp_1 \wedge de_1, \quad H = \pi e_1 + \frac{p_1^2}{2c} - c_0 + \left(c_0 - \frac{3}{2} \pi e_1\right) (e_1 \cdot e_1 - 1), \quad (3.12)$$

with the following set of constraints:

$$e_1 \cdot e_1 - 1 \approx 0, \quad p_1 \cdot e_1 \approx 0, \quad \pi e_1 + \frac{p_1^2}{2c} - c_0 \approx 0. \quad (3.13)$$

The extrinsic curvatures looks as follows:

$$\kappa_1 = \sqrt{\frac{p_1^2}{c^2}}, \quad \kappa_2 = \frac{1}{c^2 \kappa_1^2} \left(\pi^2 - 4c_0 \pi e_1 + \frac{3}{4} (\pi e_1)^2 + c_0^2\right) - \kappa_1^2. \quad (3.14)$$

The evolution equations for these curvatures could be straightforwardly obtained by the use of Poisson bracket relations \((3.7)\). They will obviously depend from the Riemann tensor \((3.8)\). We suppose to present the detailed study of the WLC model in a forthcoming paper.

4 Discussion

The statistical mechanics of the WLC has been developed by regarding it as a differentiable space curve of fixed length \([9, 11]\). If $r(s)$ is the radius vector of an arbitrary point of the curve as a function of the contour distance $s$ from one end to that point, persistence length $l_p$ can be defined as a correlation length of the tangent vectors fluctuations \([9]\)

$$(u(s)u(s + r)) \sim e^{-r/l_p}, \quad (4.15)$$

where $u(s)$ is the unit vector tangential to the curve at the point $s$. Thus, $l_p$ is statistical quantity strictly dependent on the set of available chain conformations. It is well known that the intra-chain interactions, e.g. electrostatic repulsion \([29]\) or geometrical restrictions imposed on the chain conformation \([17]\) renormalise persistent length $l_p$. However, these particular issues addressed before could not provide the systematic approach to the influence of interactions and external fields on the flexibility and elasticity of macromolecules.

In our opinion just the artificial separation of the terms describing chain elasticity and external fields or interactions presented in \([15]\) results to the strong necessity of the persistence length renormalization. Besides of artificial renormalization of the persistence length the commonly used additive scheme produced numerous inconsistencies with the description of chain flexibility. For example, stretching experiments with dsDNA of length about 0.6 – 7 $\mu$m produced the resulting fitted value for the persistence length depended on the contour length of the dsDNA \([30]\). The elastic energy of highly bent dsDNA conformations is lower than predicted by WLC model \([31]\). The list of inconsistencies can be continued.

The proposed above approach permits to take into account the external fields (or interactions) effect on the chain rigidity and elasticity directly without to invoke the artificial renormalization of persistence length $l_p$ and promised to extend our understanding of the physical properties of biological macromolecules. It consists in the introduction of the effective metrics depending on the potential of the external field, with further re-definition of the arc-length parameter and of the extrinsic curvatures of the chain. These redefinitions obviously can be interpreted as an impact of the external field in the internal energy of macromolecules, and in the natural changes of the persistent length. The proposed way to address the effect of the external fields on the conformational
statistics of macromolecules seems to be much more general than commonly used. Surely, we do not get any concrete prediction on the physical relevance of the suggested coupling. But we believe in its correctness, since it was suggested in a first principles in accordance with quite general symmetry considerations, and from this point of view, can not be wrong. While common scheme of counting external field influence coupling is pure heuristic one, and has no any motivation, except formal simplicity (or analogy with nonrelativistic mechanical systems). Moreover, any other coupling scheme, based on the “microscopic consideration”, will be in our opinion a priori more rough and simplified, than presented one. The proposed symmetry – based approach to the external field influence is in the same spirit as Bugl and Fujita model \[10\] taking into account bending and torsion in terms of the first and second curvatures.

Technical attractiveness of the suggested DNA model insist in the with spinning particles on curved space, as well as with geometric optics. This allows us easily to evaluate qualitative properties of the systems, as well as to involve, in the study of the DNA macromolecules, the tools of symplectic and Riemann geometry, Dirac’s theory of constrained systems and of the relativistic quantum mechanics.

Acknowledgments We are grateful to Armen Allahverdyan and Vladimir Morozov for encouragement and useful comments. The work was supported by and ANSEF-2229PS grant and by Volkswagen Foundation grant I/84 496.

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