David HOLCMAN

List of Publications

Research Themes

I- Pure Mathematics

A-Singular perturbations, PDE and Global Geometry.

1-Singular perturbations and nonlinear PDE [8, 9]
2-Singular pertrubations for the first eigenfunction of positive second order operator on Riemannian compact manifolds (self-adjoint case and non-selfadjoint case) [17, 18]

B-Nonlinear Analysis on Manifolds. Riemannian Geometry.

1-Nonlinear eigenvalue problems on manifolds [1, 12]
2-The Mass theory in nonlinear PDE and the mass of manifolds with boundaries [4, 10]
3- The prescribed scalar curvature problem on complete manifold [6]
4- First order PDE on compact manifold with no boundary [12, 13]
5-Boundary of complete manifolds [24]

C-Subriemannian Geometry and Control theory

1-Wave equation with degenerate operators [15]
2-Optimal switching in dynamical systems [14]

II- Applied Mathematics

Modeling neurobiological systems

1-Modeling the dynamic of microstructures: from shape to function [11, 15, 19, 20, 22]
2-Theoritical studies of diffusion with absoption [16, 23]
3-Chemical reactions in microstructures, influence of the geometry[21, 25]

Publications

1-D.Holcman, Solutions nodales sur les variétés Riemanniennes, J. of Funct. Analys., 1999,Vol. 26 p219-245.
Non symmetric nodal solutions of nonlinear PDE with Sobolev critical growth are obtained on compact manifolds. The variational method and bifurcations theory are used to construct a branch of solution.

2-D. Holcman, Solutions nodales sur les variétés Riemanniennes compactes, Compt. Rend. Acad. Sci. Paris, 1998,t. 326, Série I, p1205-1208

3-D. Holcman, Solutions nodales d'EDP non linéaires sur les variétés non localement conformément plates, Paris 2000, Comment. Math. Helv. 76 (2001), no. 3, 373--387
This paper deals with solutions of Dirichlet problem for a nonlinear PDE with boundary data changing of sign. A family of minimizing nodal solutions are found on non locally conformally flat manifolds.

4-D. Holcman, Influence de la masse sur les solutions nodales d'EDP non linéaires, Bull. Sci. Math. 124 (2000), no. 5, 385--414
Solutions of Dirichlet problem for a nonlinear PDE with a boundary data are obtained by a variational method. A family of minimizing nodal solutions is found on compact locally conformally flat manifolds with boundary. Manifolds with boundary and positive mass are found. A combination of the mass term and the Dirichlet boundary data give sufficient condition to prove the existence of minimizing regular solutions .

5-D. Holcman, Solutions nodales sur les variétés riemanniennes à bord, Compt. Rend. Acad. Sci. Paris, t.326, Serie I, 1998, p1321-1324.

6-D. Holcman, Prescribed Scalar Curvature problem on Complete manifolds, J. Math. Pures Appl. (9) 80 (2001), no. 2, 223--244.et Appl. 2001.
Conditions on the geometric structure of a complete Riemannian manifold are given to solve the prescribed scalar curvature problem in the positive case. The conformal metric obtained is complete. A minimizing sequence is constructed which converges strongly to a solution. In a second part, the prescribed scalar curvature problem of zero value is solved which is equivalent to find a solution to a linear PDE on complete manifold. This solution helps to obtain a general result on the prescribed scalar curvature problem, in the positive case.

7-D. Holcman, Prescribed Scalar Curvature problem on Complete manifolds, Compt. Acad. Sci Serie I,t 328, 1999. p 321-326.

8-D. Holcman, Nonlinear PDE with vector fields, J. Anal. Math. 81 (2000), 111--137.
We study on a compact manifold, a nonlinear PDE, with a given vector field. The nonlinear term involves the Sobolev critical exponent growth. To obtain the existence of solutions, conditions linking a critical point of the field and the scalar curvature are found. The second section is devoted to study the limit of a sequence of PDE with a viscosity parameter tending to zero.

9-D.Holcman, EDP non linéaires avec champ de vecteurs, Compt. Rend. Acad. Sci. Paris, 1999.

10-D. Holcman, On the mass of manifolds with boundary, C. R. Acad. Sci. Paris Sér. I Math. 328 (1999), no. 12, 1191--1196
The mass of compact manifolds with boundary is studied. This number is defined as the constant part of the Green function of the conformal Laplacian in the usual asymptotically development. The main result is the following: under some assumptions the mass of a compact locally conformally flat manifold with boundary is negative.

11- Barrie J.M., Holcman D., Freeman W.J., Statistical evaluation of clusters derived by nonlinear mapping of EEG spatial patterns, Journal of Neuroscience Methods august(90) 1999 p87-95.

12-D. Holcman E. Humbert, Poincare-Sobolev inequality on manifolds with boundary, Math. Z. 237 (2001), no. 4, 669--695
We propose to study in this paper inequalities of Poincare Sobolev type on manifolds with boundary in the case of a critical Sobolev exponent. We deduce from the existence of a minimizing solution to a variational problem an upper bound of the first best constant involved in this inequality. The upper bound depends on some geometrical quantities (volume, diameter, second fundamental form, curvature and Ricci curvature).

13-D. Holcman I. Kupka, Singular Perturbation and first order PDE on manifolds. C. R. Acad. Sci. Paris Sér. I Math. 333 (2001), no. 5, 465--470.
In the first part of this paper, we study the concentration of the sequence of the first eigenfunctions on the limit sets of a Morse-Smale dynamical system. In the second part, certain aspects of some first order PDE on manifolds are studied. We study the limit of a sequence solutions of a second order PDE, when a parameter of viscosity tends to zero. Under some explicit assumptions on some vector fields, bounded and differentiable solutions are obtained. We exhibit the role played by the limit sets of the dynamical systems and provide in some cases an explicit representation formula.

14-D. Holcman I. Kupka, Perturbation Methods and First Order Differential Equations, accepted Quaterly Journal Math.
In this paper, we give explicit estimates that insure the existence of solutions for first order partial differential operators on compact manifolds, using a viscosity method. In the linear case, an explicit integral formula can be found, using the characteristics curves. The solution is given explicitly on the critical points and the limit cycles of the vector field of the first order term of the operator. In the nonlinear case, a generalization of the Weitzenbock formula provides pointwise estimates that insure the existence of a solution, but the uniqueness question is left open. Nevertheless we prove that uniqueness is stable under a C^1 perturbation. Finally, we give some examples where the solution fails

to exist globally, justifying the need to impose conditions that warrant global existence. The last result reveals that the zero order term in the first order operator is necessary to obtain generically bounded solutions.

15-D.Holcman M.Margaliot, Stability Analysis of Switched Homogeneous Systems in the plane, SIAM J. of Control, Jan 2003.
We present a new approach to analyze the stability of switched homogeneous dynamical systems in the plane. We focus on nonlinear homogeneous systems. We will see that it is possible to reduce the problem of switching between the solutions of the dynamical systems to the study of the level line of a quantity which extends to the all plane, the standard notion of first integral. We obtain in this way a necessary and sufficient condition to insure the existence of a stabilizing feedback controller which can be easily computed. Finally we use this stability analysis to solve the problem of designing a feedback controller that stabilizes a planar homogeneous system.

16-P. Greiner D. Holcman Y. Kannai, Wave Kernel related to second order operators, Duke Mathematical Journal, September 2002.
The wave kernel for a class of second order sub-elliptic operators is explicitly computed. This class contains degenerate elliptic and hypo-elliptic operators (such as the Heisenberg Laplacian and the Grusin operator). Three approaches are used to compute the kernels and to determine their behavior near the singular set. The formulas are applied to study propagation of the singularities. The results are expressed in terms of the real values of a complex function extending the Carnot-Caratheodory distance, and the geodesics of the associated sub-Riemannian geometry play a crucial role in the analysis.

Publications Submitted

17-D.Holcman A. Marchevska Z. Schuss, The survival probability of diffusion with killing.
We consider the long time behavior of the survival probability of a Brownian trajectory on the real line and in a finite interval with a killing measure supported in various sets. We show that the asymptotic decay of the survival probability depends on the structure of the support of the killing measure. We find both exponential and algebraic decays of the survival probability. We consider, in particular, measures supported on discrete sets. We show that killing at one point gives a different decay rate than that at two points with the same weight. These results also determine the probability distribution of the time spent by Brownian motion in a given set. The model may represent diffusion of ions in the presence of proteins containing binding sites.

18-D. Holcman I. Kupka, Semi-classical limit of the first eigenfunction and concentration on the recurrent sets of a dynamical system.
On compact Riemannian manifolds, we study the semi-classical limit of the first eigenfunction of a positive second order operator, as a small parameter goes to zero. When the first order term of the operator is a Morse-Smale vector field b, subsequences of eigenfunction concentrate on subsets of the recurrent sets. Near the recurrent sets, the properties of the limit measures are studied by a blow-up analysis: the support of the measures is the same as the one obtained by using the variational formulation of the topological pressure equals to the limit of the first eigenvalue sequence. When b has limit cycles, we prove that the limit measure is absolutely continuous with respect to the limit cycle Riemannian length. When the limit measure is supported by several cycles, under some conditions, the relative weight is computed explicitly. The concentration of the eigenfunction sequences occurs on the recurrent sets of maximal dimension, where the topological pressure is achieved. Under additional assumptions, when the recurrent sets of b contain several two-dimensional hyperbolic torus, the limit measures can be concentrated on the torus where the topological pressure is achieved. In that case when b restricted to the torus is conjugated to an ergodic field, the limit measure is absolutely continuous with respect to the area.

19-D. Holcman Z. Schuss, Modeling Calcium Dynamics in Dendritic Spines.
A dendritic spine is a cell-like structure located on a dendrite of a neuron. It conducts calcium ions from the synapse to the dendrite. A dendritic spine can contain anywhere between a few and up to

thousands of calcium ions at a time. Internal calcium is known to bring about fast contractions of dendritic spines (twitching) after an action potential or a back-propagating action potential. In this paper, we propose a coarse-grained reaction-diffusion (RD) model of a Langevin simulation of the twitching. The RD equations couple the contraction of proteins to the chemical reaction. The calcium induced contraction of actin-myosin-type proteins produces a flow of the cytoplasmic fluid in the direction of the dendritic shaft, thus speeding up the time course of calcium dynamics in the spine, relative to pure diffusion. Experimental and simulation results reveal two time periods in spine calcium dynamics. In the first period calcium motion is mainly driven by the hydrodynamics, while in the second period it is mainly diffusion. The coarse-grained RD model also gives this result.

20-D. Holcman J. Korenbrot, Longitudinal diffusion in retinal rod and cone outer segment : the role of cytoarchitecture.
The longitudinal diffusion in Cones and Rods outer-segment is analyzed both theoretically and experimentally. The analysis reveals that longitudinal diffusion in cone satisfies a new diffusion equation, due to the non uniform geometry, whereas in rod the equation is linear. The model is validated by the experiments. As a consequence, the spread of excitation due to a single photon response is predicted.

21-D. Holcman, Z. Schuss, E. Korkotian, Calcium dynamics in dendritic spines and spine motility.
Dendritic spines, the locus of excitatory synaptic interaction in central neurons constitutes a unique intracellular calcium compartment, in that it can raise $[Ca^{2+}]$ to levels higher than those of the parent dendrite. A transient rise of internal calcium can bring about a fast twitch of dendritic spines, the function of which is still unclear. We propose an explanation of the cause and effect of the twitching and its role in the functioning of the spine as a fast calcium compartment. In the present molecular model of calcium dynamics, the rapid calcium motility is due to the concerted contraction of calcium-binding proteins. The contraction induces a stream of the cytoplasmic fluid in the direction of the dendritic shaft, thus speeding up the time course of spinal calcium dynamics, relative to pure diffusion. The simulation indicates that spine motility can be explained by the basic rules of chemical reaction rate theory at the molecular level. Analysis of the simulations reveals two time periods in the calcium dynamics. The model proves that the role of rapid motility in dendritic spines is to increase the efficiency of calcium conduction to the dendrite and to speed up the emptying of the spine.

Publications in Preparation

22-D. Holcman I. Kupka, Singular perturbation for the first eigenfunction and blow up analysis, pre-print.
On a compact Riemannian manifold (V_m, g), we consider the second order positive operator $L_\varepsilon = \varepsilon \Delta_g + (b, \nabla) + c$, where Δ_g is the Laplace-Beltrami operator and b is a Morse-Smale (MS) field, ε a small parameter. We study the measures which are the limits of the normalized first eigenfunctions of L_ε as ε goes to the zero. In the case of a general MS field b, such a limit measure is the sum of a linear combination of Dirac measures located at the singular point of b and a linear combination of measures supported by the limit cycles of b. When b is a MS-gradient vector field, we use a Blow-up analysis to determine how the sequence concentrates on the critical point set. We prove that the set of critical points that a critical point belongs to the support of a limit measure only if the Topological Pressure defined by a variational problem is achieved there. Also if a sequence converges to a measure in such a way that every critical points is a limit point of global maxima of the eigenfunction, then we can compute the weight of a limit measure. This result provides a link between the limit of the first eigenvalue sequence and the associated first eigenfunction sequence. We give an interpretation of this result in term of the movement of a Brownian particle driven by a field and subjected to a potential well, in the small noise limit.

23-D. Holcman Z. Schuss, Kinetics of Non-Arrhenius reactions, pre-print.
Chemical kinetics of some reactions in micro-biological structures, where equilibrium can not be assumed, are described by new equations. They are derived from a Langevin description of diffusing particles in the presence of a substrate, such as cell proteins. The evolution of substrate and reactant

concentrations take into consideration their initial relative distributions and the geometry of the domain. The proposed theory is sufficiently general to model transient processes occurring in neurobiological micro-structures, where the number of involved particles is in between a few, modelled with sufficient accuracy by stochastic theory of discrete particles, and a large population that can be described by standard deterministic continuum theory.

24-D. Holcman, Z. Schuss, Theory of confinement time and lateral diffusion of receptors in postsynaptic membrane, pre-print .
We compute the mean exit time that a receptor takes to exit a bounded domain, through a small region of the boundary. This time is call the confinement time. Explicit formula are obtained by a singular perturbation analysis of a mixed boundary value problem. This problem is related to the mean time a channel (AMPAR) spent into a coral zone of the postsynaptic density, before leaving.

25-D. Holcman, C Pugh, The boundary between compact and noncompact Riemann manifolds, pre-print.
There should be a boundary in the space of Ricci curvature functions with all compact manifolds on one side and all non-compact complete manifolds. Sufficient conditions on the decay of the Ricci curvature are presented that imply compactness. The conditions are close to be optimal.

26-D. Holcman, Z. Schuss, A theory of stochastic chemical reactions in confined microstrucures, pre-print.
Stochastic chemical reactions in micro-domains are described by a set of new partial differential equations, generalizing the standard reaction-diffusion equations. As a consequence the fluctuation in the chemical reactions can be estimated. The fluctuation term represents the binding and unbinding of molecules to the substrate and depends on the geometry of the domain and the distribution of the proteins inside the domain.

Ongoing projects-2003-2004

- **Modeling the dynamic of photo-tranduction,** coll. J. Korenbrot (UCSF).

27-The single photo-response curve is based at a molecular level. Using a Langevin model in specific cell geometry, a new Fokker-Planck equation is derived. The time difference in the response curve can be estimated for cones versus rods.

28- The origin of the dark noise in retinal cells is investigated using a stochastic chemical reaction theory.

- **Spontaneous activty of the area V1 of the visual cortex,** coll. K. Miller and T. Kenet (UCSF)

29-A stochastic dynamical system based on synaptic connections is presented to explain and predict spontaneous activity in area V1 of the visual cortex.