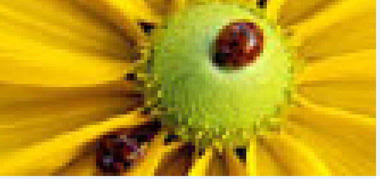
# A Numerical Approach for Multi-Scale Biomedical Problems

Marc Garbey[(1)], Christophe Picard[(1)], Francois Pacull[(2)]
and Roger Tran-Son-Tay[(3)]

(1) Dept. of CS, UH

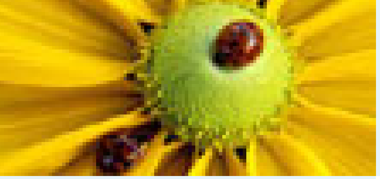
(2) Dept. of Math, UH

(3) Dept. of Mechanic and Aerospace Engineering, UF





# Introduction



# Introduction



**Goal**

- To develop numerical tools useful for the understanding of fundamental phenomena in Blood Flow, including some biochemistry and cellular dynamics.
- Open problem that *may* benefit from multi-scale tools: understanding the relation ship between inflammation and cholesterol plaque.

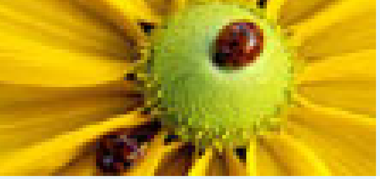
**Corresponding Topics in Applied Mathematic**

- Heterogeneous Domain Decomposition for Multi-Scale Problem.
- Fluid-Structure Interaction in the Boundary Layer.
- Immersed Boundary Method (IBM) (ref. C.Peskin)

# Plan of the talk



- Bio-Medical Motivation.
- A General PDE framework for Modeling.
- Domain Decomposition and Singular Perturbation.
- Fluid Structure Interaction with IBM.

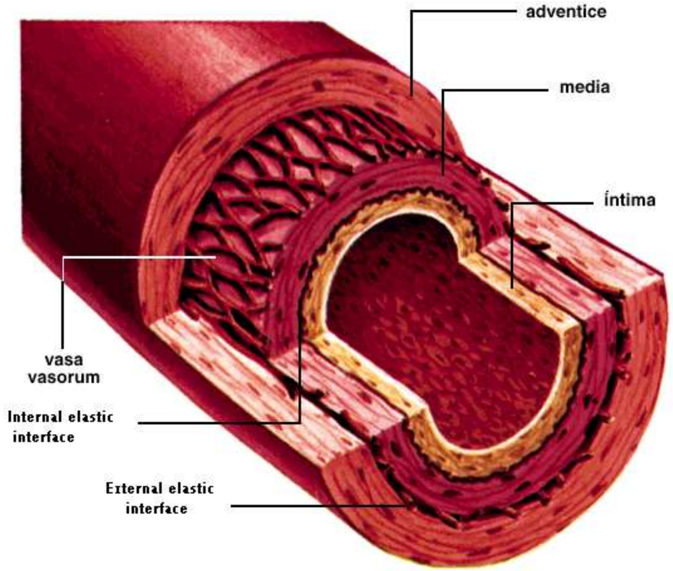


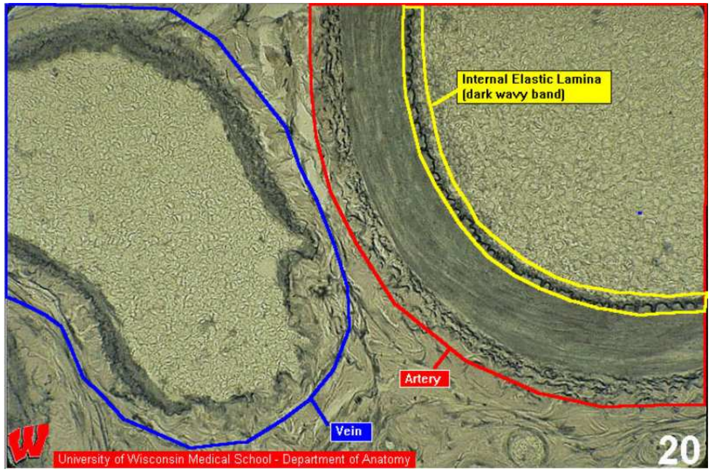


# Bio-Medical Background

# Simplified Structure of an Artery



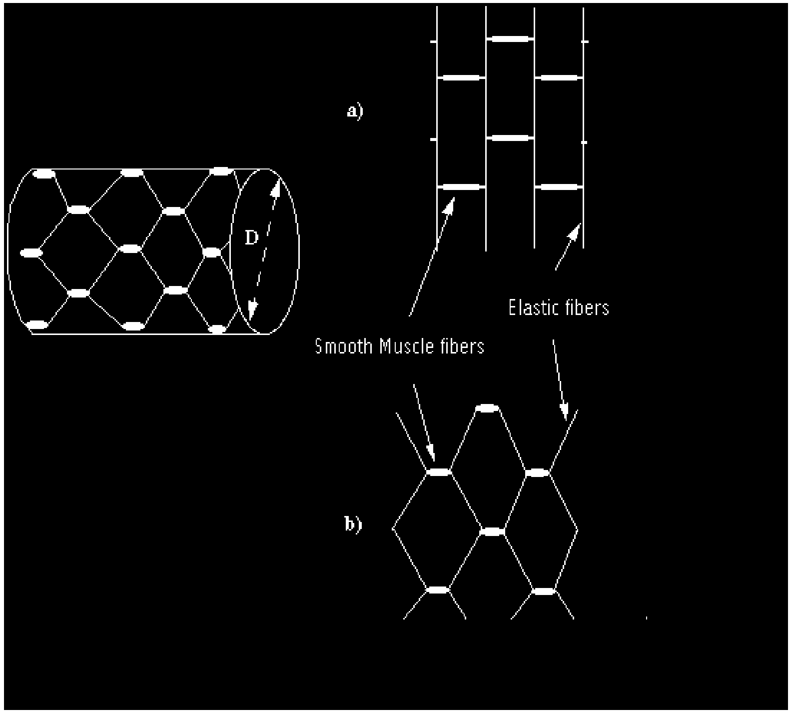


# Mechanical Properties of the Artery Wall

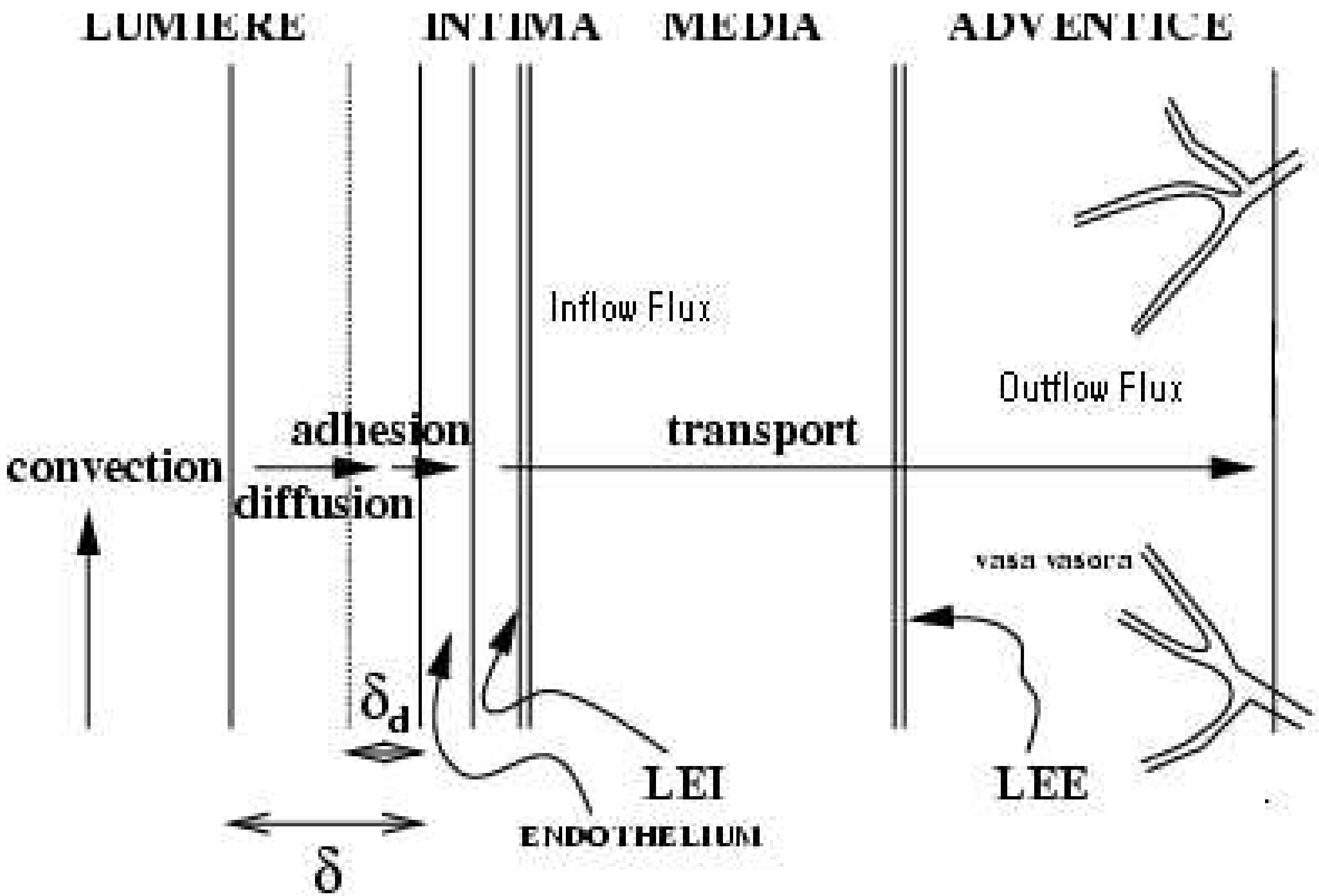


- Tunica media: responsible for the elastic properties of arteries.
- Complex network of elastic fibers and muscle fibers for dilatation and contraction.
- Ratio of elastic fibers/ muscle fibers depends on the distance of the artery section to the heart.
- Structure varies depending on the healthiness of the artery.



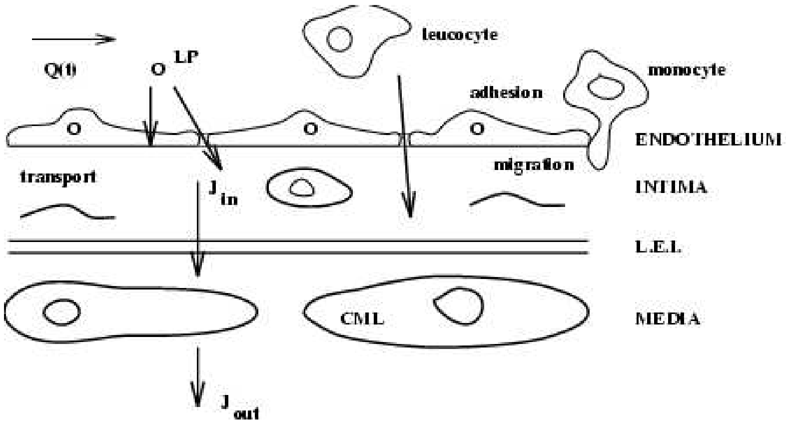
# Diffusion-Convection-Reaction





# Modeling of the Intima for Wall Absorption.



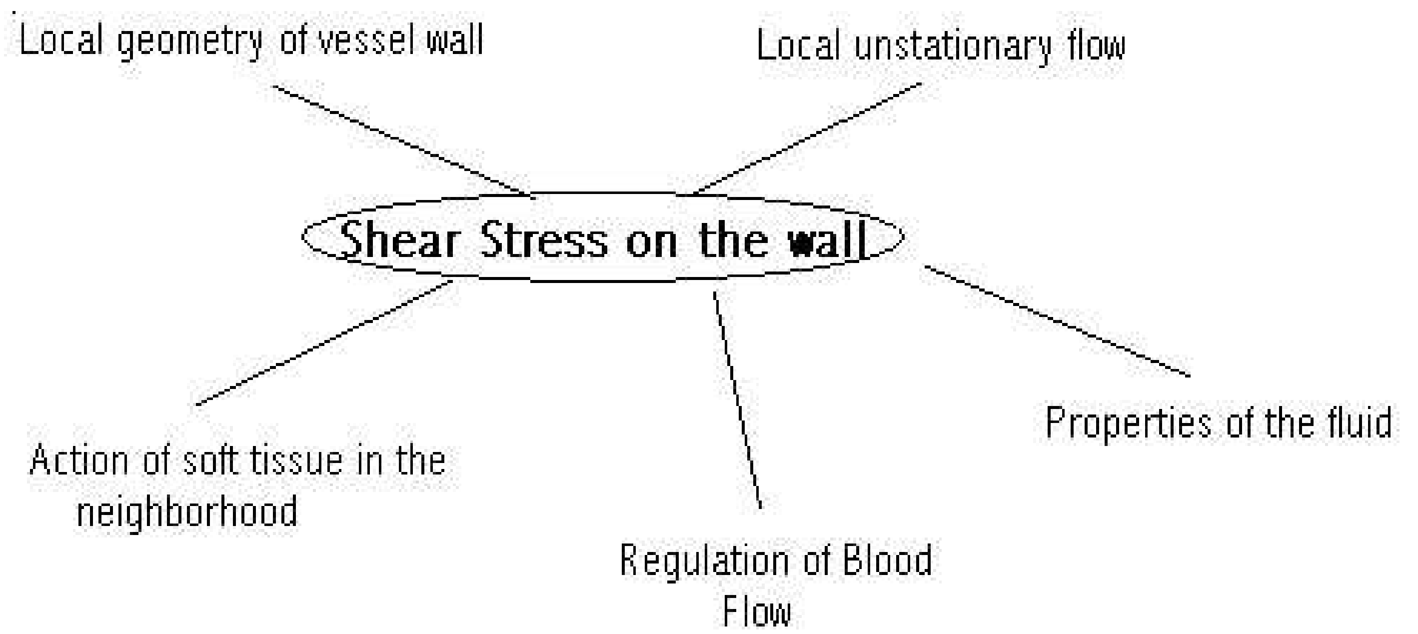



- The mono-cellular layer of endothelium can be considered as a porous membrane for some chemical components, with permeability depending on the specific components.

- Externa tunica anchors the vessel to the body, but has also a fundamental role in biochemical exchanges with the environment of the artery.

# Shear Stress





# A General PDE Framework for Modeling

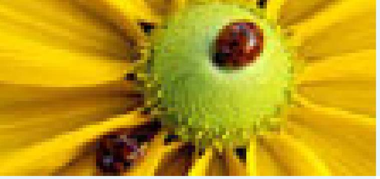
# PDE Framework for Arteries



- Incompressible Navier Stokes Equations (NS) is a good approximation for blood flow in artery of diameters larger than one or two millimeters.
- Darcy Law in the wall - P. Zunino et Al 02.
- Reaction-Convection-Diffusion in Lumen + Wall:

$$\partial_t C + \nabla.(uC) = \nabla.(D\nabla C) + Q(C, E, t) \quad ,$$

  where $C$ is a vector of chemical components, $D$ stands for the solute diffusivity.
- $D$ is usually a diagonal matrix $(d_i)$ with coefficients that have large discontinuities across the interfaces that separates several tissue layers.
- The source term $Q$ can be a source or a sink attached to the wall location.



# IBM Approach



A body force $F$ in the momentum equation for:

- Fluid-Structure Interaction: - ref. Peskin - when the wall is assimilated to a network of elastic and muscle fibers:

$$F(x,t) = \int_0^L f(s,t)\delta(x - X(s,t))ds \quad ,$$

  - $X(s,t)$ is the time dependent location of the fiber, $\delta$ is the Dirac function,
  - $f(s,t)$ describes the elastic properties of the fiber,
  - $\frac{\partial X}{\partial t}(s,t) = u(X(s,t),t)$ is the no-slip boundary condition.

- Elastic-contractile properties of the smooth muscle fibers might be modulated by concentration of vasoactive agents.
- Eventually add a damping factor to simulate the anatomical structures and intersticial matrix external to the vessel.

# IBM Approach II



Interactions between platelets or adhesion of particles to the wall -ref Fogelson-

$$\partial_t E + u.\nabla_x E + (v.\nabla u).\nabla_v E = R(C, E, t) \ ,$$

- Two space scale description expressed by a bond density $E$,
- $v$ represents the microscale space variable,
- $R$ is an appropriate source term to express creation and destruction of bonds.

**In vivo data of the model?**

**What are the solvers required for this general framework?**

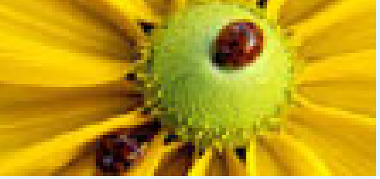
# PDE solvers



$$\partial_t U + (\vec{a}.\nabla)U - \nabla.(D\nabla U),\ ||D|| << \epsilon$$

$$div(K\nabla U),$$

- $U$ is a vector, $K$ may have large jump at interfaces.
- RHS can be a set of Dirac or Dipoles.
- Asymptotic Induced Domain Decomposition Method. MG Sisc 96.
- Heterogeneous DD for these two solvers. ref MG and H.Kaper Sinum 97.
- Multigrid and tau extrapolation method for Elliptic Pb with singular source terms - U.Ruede. F.Pacull and MG DD16.
- A posteriori Error estimate. MG and W.Shyy 05.



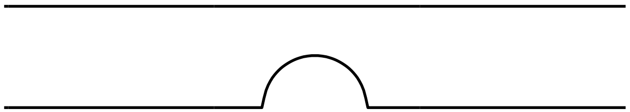
# Fast Prototyping of NS flow (1)



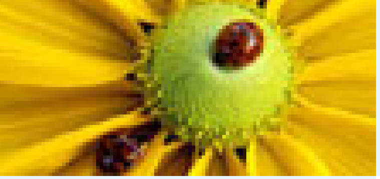
$$\partial_t U + \mathcal{H}(\vec{U}.\nabla)U - \nu\nabla.(\nabla U) = -\frac{1}{\eta}\Lambda_{\Omega_s}\ \{U - U_s(t)\},$$

$$div(U) \ = \ 0,$$

- $\Omega_s$ solid wall.
- $U_s(t)$ speed of the wall.
- $L^2$ Penalty method: $\eta >> 1.$ - reference Caltagirone 84, Bruneau et al 99., Schneider et al 2005-
- $\mathcal{H}$ smooth cutt off function to match NS with Stokes flow at inlet/outlet.

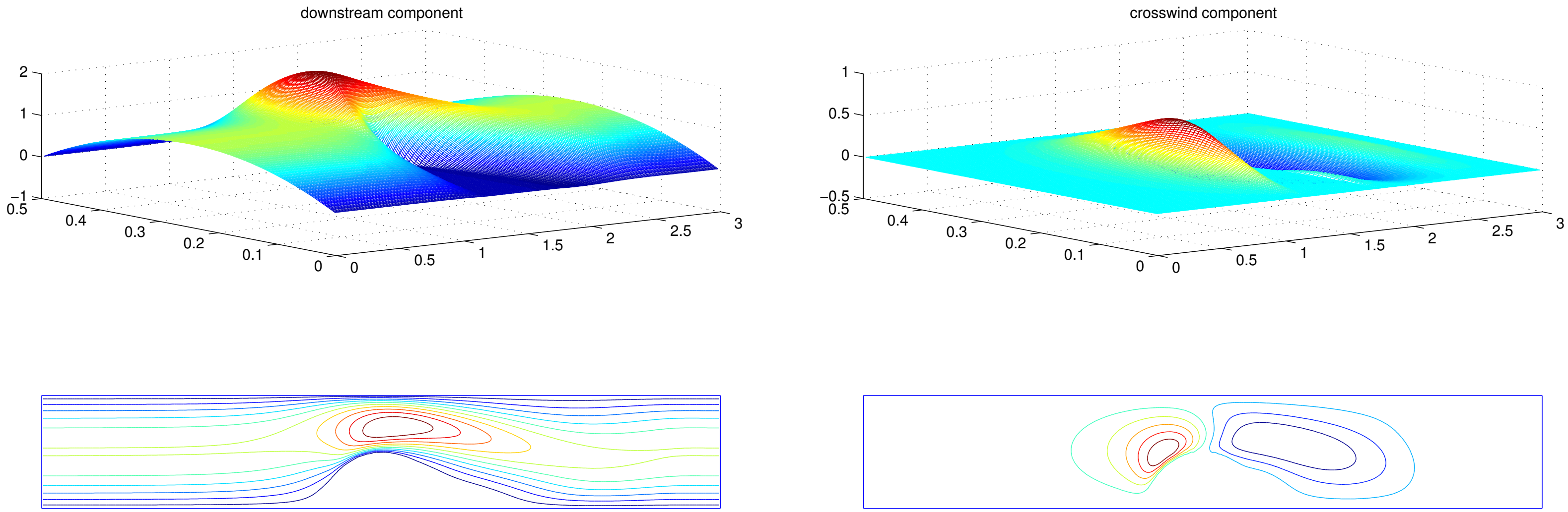


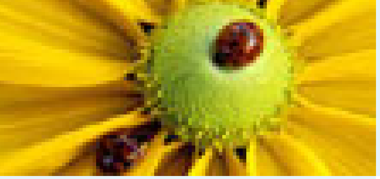
$$Lx = 3, Ly = 0.5, \nu = 0.01; h_y = 2/3h_x.$$



# Fast Prototying of NS flow (2)

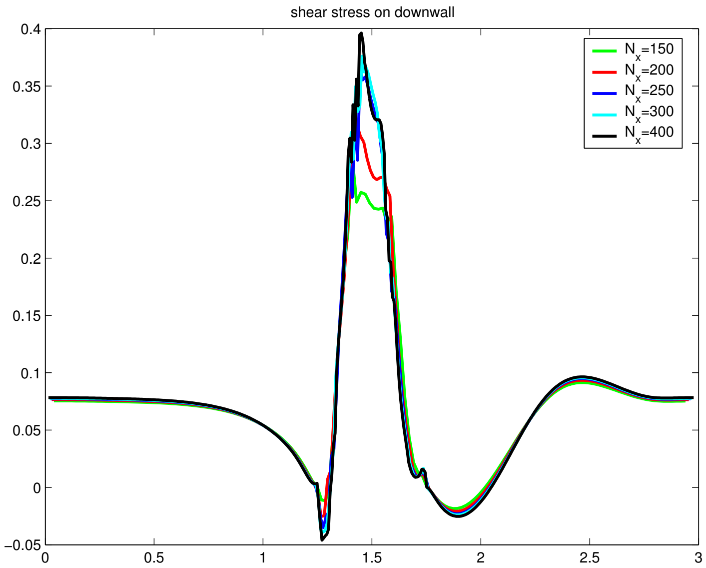


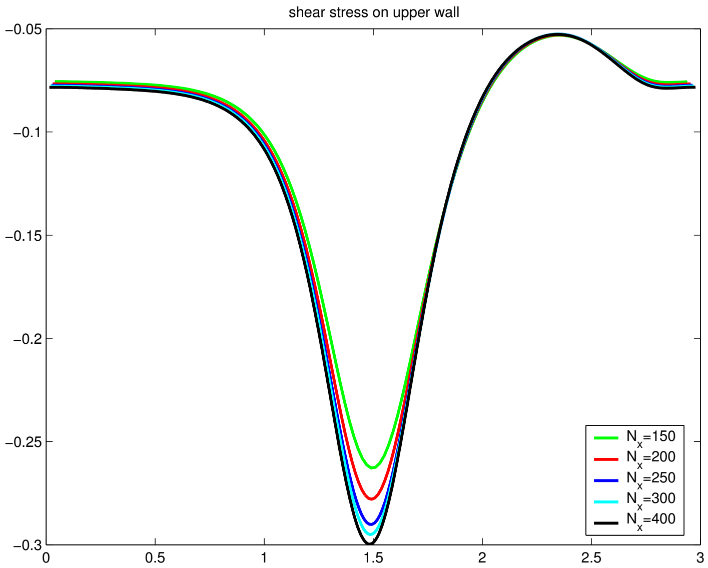




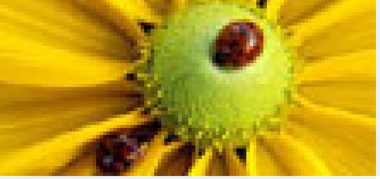
# Fast Prototying of NS flow (3)





# Domain Decomposition and Singular Perturbation



# Matched Asymptotic Expansion method ?



W.Eckhaus, O'Malley, Kevorkian etc...

- The domain $\Omega$ should be decomposed into $\Omega = \Omega^R \cup \Omega^{BL}$.
- Choice of the space variable should provide regular asymptotic expansion:

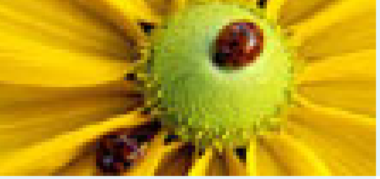
$$U^R = \sum_{i=1..n} \delta_i^R(\epsilon) U_i^R, \; U^{BL} = \sum_{j=1..m} \delta_j^{BL}(\epsilon) U_j^{BL},$$

- Local orthogonal coordinate system $\rho, \eta$ in $\Omega^{BL}$ attached to the wall $\partial\Omega$, with normal-tangential coordinates.
- Normal variable should be stretched as $\xi = \frac{\rho}{\epsilon^p}$, according to **the thickness of the layer.**
- Matching conditions define a consistent composite uniform expansion:

$$U = \mathcal{H}\, U^R + (1 - \mathcal{H})\, U^{BL},$$

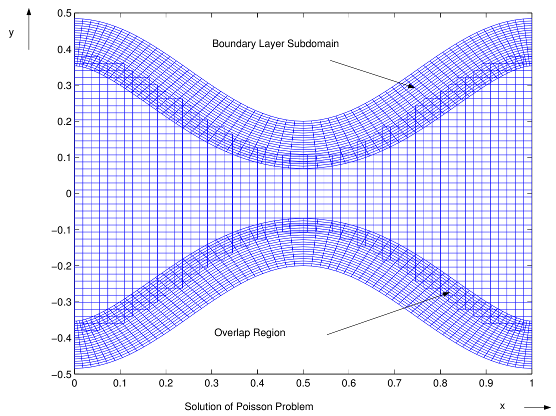
where $\mathcal{H}$ is a partition of unity.

- Stability estimate necessary to prove the convergence.



# From Asymptotic to Numeric?





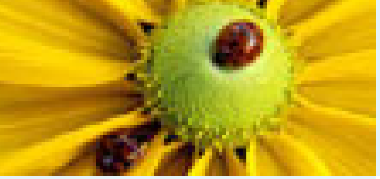

- Difference in space scaling is taken care by the DD.
- Artificial interfaces associated to BL may give superlinear cge.
- Regular Data structures imply efficient use of the cache.

- Background Cartesian grid for $\Omega^R$, can be used as a preconditioner with fictitious DD - ref G.Marchuk et Al 86 -.
- The Schwarz algorithm leads to the matching condition (if maximum principle satisified).
- Operator: First order asymptotic approximation might be a good preconditioner.

# Some Difficulties

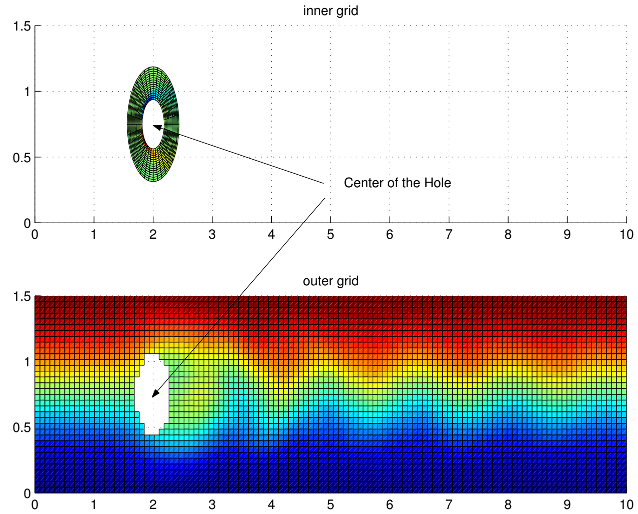


- **Conservativity:**
  - interface conditions should be conservative in some sense ...see G.Chesshire and W.Henshaw.
  - "Heuristic": if the problem is smooth enough, i.e if we resolves the boundary layer scale, accuracy is fine....even when conservation is not enforced.
- **System of Coupled PDEs**
  - The Schwarz algorithm might be very slow for the elliptic Pb, for example the pressure equation in NS: typically $90$ per cent of the overall elapsed time !
  - **Aitken-Schwarz algorithm:** An approximate reconstruction of the dominant eigenvectors of the trace transfer operator can accelerate the Schwarz sequence -ref MG and D Tromeur Dervout Int.J. Num. Method in Fluid 2002- MG SISC 2005.

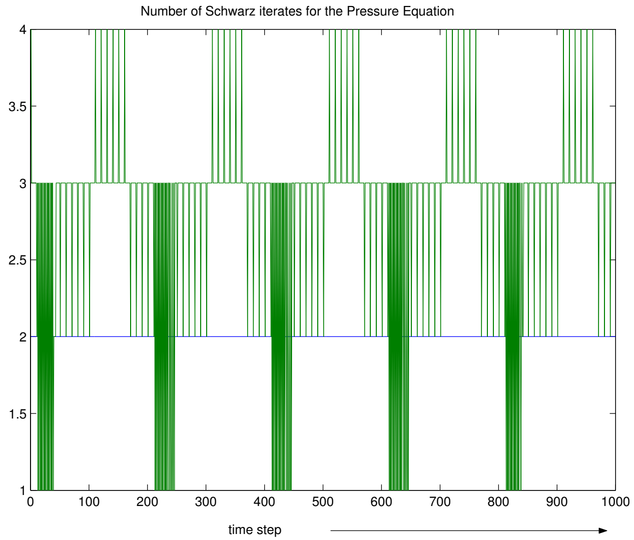


# Heterogeneous DD for NS

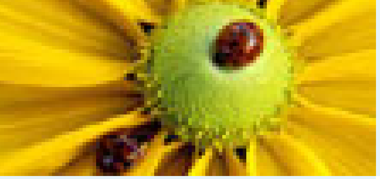





Composite mesh for a two D flow past a cylinder in a long channel.




Number of Schwarz iterates for the stream solution procedure as function of time step's number.





# Immersed Boundary Method

# The discrete Dirac delta function $\delta_h$



$$\delta_h(x) = \frac{1}{h}\phi(\frac{x}{h}).$$

- $\phi$ needs to satisfy several compatibility conditions.
- Engquist and Tornberg showed that the discretization error is proportional to the number of moment conditions satisfied by the function.

$$\phi(r) \quad = \quad \begin{cases} 1-\frac{1}{2}|r|-|r|^2+\frac{1}{2}|r|^3, & 0 \leq |r| \leq 1; \\ 1-\frac{11}{6}|r|+|r|^2-\frac{1}{6}|r|^3, & 1 < |r| \leq 2; \\ 0, \ \text{otherwise.} & \end{cases}$$

- We use extensively this new discretization of the $\delta$ function, adapted to the staggered meshes.

# The multigrid $\tau$–extrapolation



The $\tau$–extrapolation - Bernert97, Rude04 - is a modified multigrid method that improves the convergence order of a discrete problem:

- It is based on the Richardson extrapolation technique.
- It combines two solutions obtained on different grids in order to correct the fine grid solution.
- Convergence order might be evaluated experimentally.
- The support of the dirac delta function changes with the coarsening.

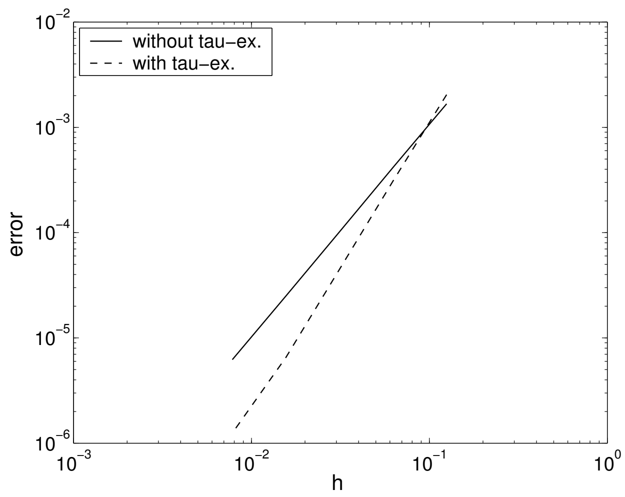
# Benchmark Problem:



$$-\Delta u(x,y) = \delta(x,y,\Gamma), \quad (x,y) \in \Omega = [-1,1]^2; \tag{1}$$

$$\Gamma = \left\{(x,y) \in \Omega / x^2 + y^2 = r^2\right\}, \quad r < 1, \quad u_{|\partial\Omega} = u_{ex|\partial\Omega}$$

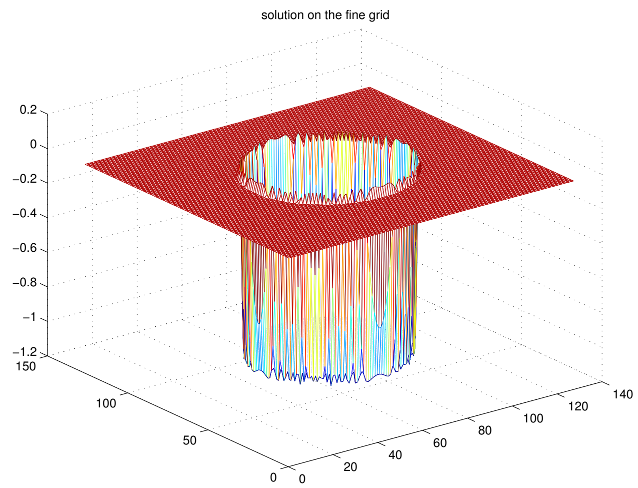
$$u_{ex}(x,y) = \begin{cases} 1 - \frac{1}{2} ln\left(\frac{1}{r}\sqrt{x^2+y^2}\right), & \text{if} \quad x^2+y^2 > r^2; \\ 1, & \text{if} \quad x^2+y^2 \le r^2. \end{cases}$$




Error in L2-norm of the method for the multigrid algorithm with or without the $\tau$–extrapolation and using the piece. cub. delta func. The order is improved from 2.0 to 2.8.

# Benchmark Problem with dipoles

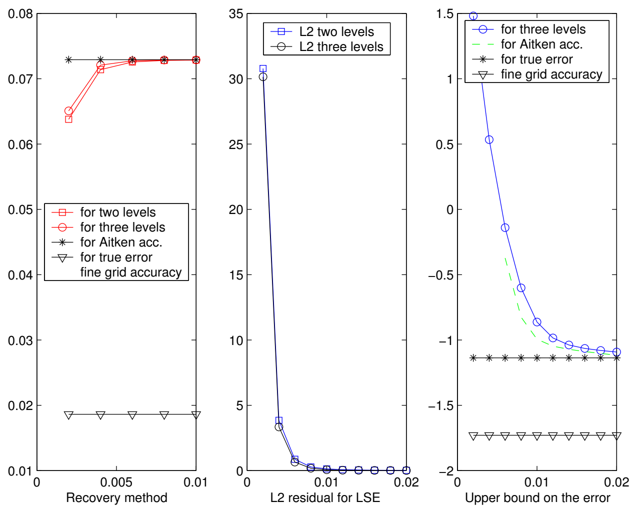




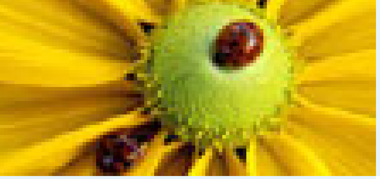

Solution of the Poisson Problem with a circle of dipoles source terms.

# Benchmark Problem: A Posteriori Error



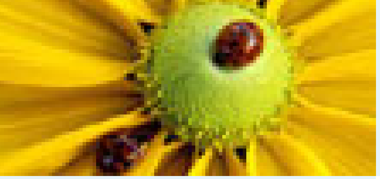



Error estimates in $L_2$ norm based on the Least Square Extrapolation Method. MG and W.Shyy JCP 03, Int. J. for Num. Methods in Fluids 05.





# Conclusion



# Few Items



1. Each sub-domain can use a fast solver that takes full advantage of either the stretching of the mesh in one space direction for boundary layer domains, or the regular data structure with Cartesian grids used for the main part of the flow.
2. Simplicity of the implementation, grid generation, and memory allocation due to the use of the Schwarz method for the iteration process between overlapping non matching grids.
3. Fast convergence of the domain decomposition algorithm thanks to the use of an acceleration procedure to speed up the convergence of the Schwarz method.
4. Biologically motivated domain decomposition !
5. IBM framework well adapted to biological problems.
6. To be done: more biology, more image analysis....