

# Optimizing the Kelvin force in a moving target subdomain

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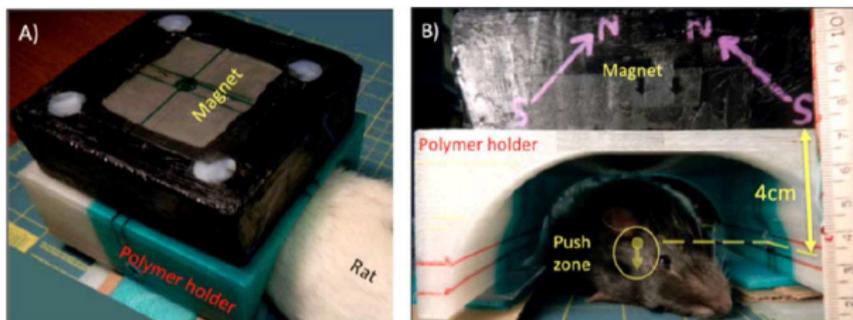
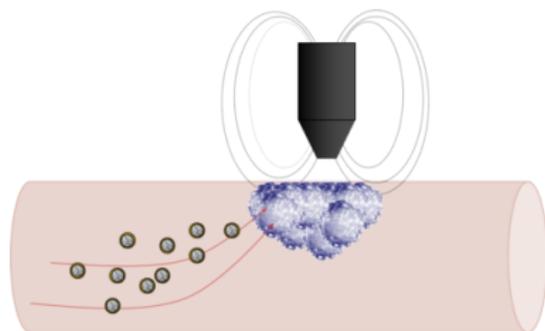
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# Motivation

The magnetic field exerts a force on magnetic materials such as magnetic nanoparticles (MNPs). MNPs under the action of external magnetic field are used in:

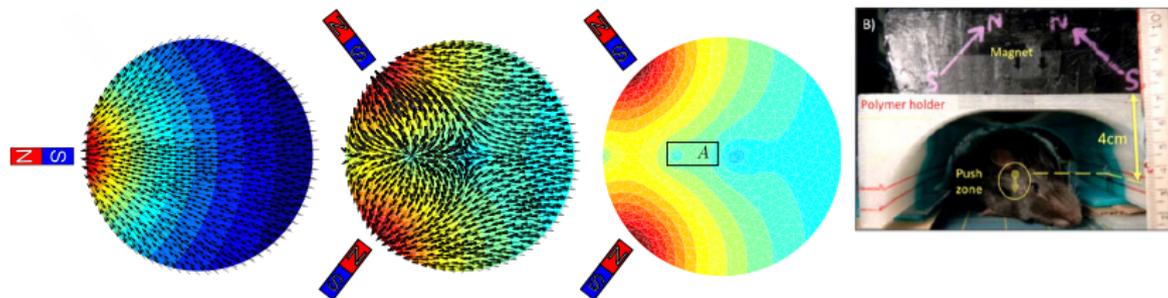
- ▶ medical sciences:
  - ▶ as contrast agents to enhance the contrast in MRI
  - ▶ as carriers for targeted drug delivery, for instance, to treat cancer cells, tumors ( $< 0.1\%$  is taken by tumor cells)
  - ▶ in gene therapy
  - ▶ in magnetized stem-cells
- ▶ magnetic tweezers
- ▶ lab-on-a-chip systems that include magnetic particles or fluids
- ▶ magnetofection a transfection method

# Magnetic drug targeting (MDT)



Experimental setup ([Shapiro et al., 2013])

# What are engineers interested in?



- ▶ Pull in or attract particles (left): there are already human trials on this.
- ▶ **Key difficulty:** To push or to control particles (center and right). In region  $A$  the force is pointing outward, allowing us to push particles.
- ▶ The success of the aforementioned applications highly depend on the **accurate control of the magnetic force**.
- ▶ **Goal:** how to approximate a desired magnetic force  $\mathbf{f}$  by a fixed configuration of magnetic field sources.
- ▶ **Approach:**

$$\min_{\mathbf{F}} \int_0^T \|\mathbf{F} - \mathbf{f}\|_{L^2(D)}^2 dt \quad \text{for } T > 0 \text{ and } D \subset \mathbb{R}^d, d = 2, 3.$$

# How does magnetic field manipulate MNPs?

- ▶ **Magnetic force:** Magnetic field gradient is required to exert a force and such a force is given by [Rosensweig '97]:

$$\mathbf{F} = (\mathbf{m} \cdot \nabla)\mathbf{H}.$$

- ▶ **A simplification:** After some simplifications (weakly diamagnetic medium, no current sources) and using  $\text{curl } \mathbf{H} = 0$ , the force on a single MNP

$$\mathbf{F} = \frac{V_m \Delta \chi}{2} \nabla |\mathbf{H}|^2$$

$V_m$ : is the volume of the particle

$\Delta \chi = \chi_p - \chi_m$ : effective susceptibility.

- ▶ **Fundamental difficulty:** magnetic field intensity  $\mathbf{H}$  is not parallel to the magnetic force  $\mathbf{F}$ .

# Minimization problem and control action

- ▶  $\Omega \subset \mathbb{R}^d$ ,  $d = 2, 3$  open, bounded  
 $D_t \subset \Omega$ : time dependent subdomain.
- ▶ **Maxwell's equations:** We consider magnetic sources outside  $\Omega$  then

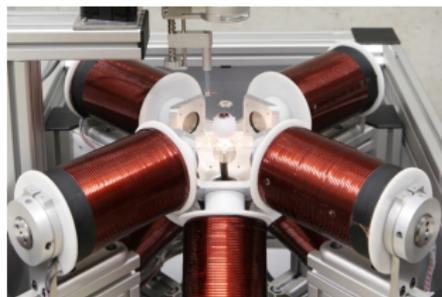
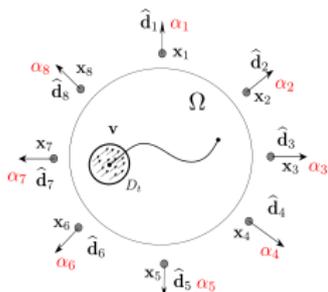
$$\operatorname{curl} \mathbf{H} = \mathbf{0}, \quad \operatorname{div} \mathbf{H} = 0 \quad \text{in } \Omega.$$

- ▶ **Dipole approximation:**

$$\mathbf{H}(\mathbf{x}, t) = \sum_{i=1}^{n_p} \alpha_i(t) \left( d \frac{(\mathbf{x} - \mathbf{x}_i)(\mathbf{x} - \mathbf{x}_i)^\top}{|\mathbf{x} - \mathbf{x}_i|^2} - \mathbb{I} \right) \frac{\hat{\mathbf{d}}_i}{|\mathbf{x} - \mathbf{x}_i|^d} = \sum_{i=1}^{n_p} \alpha_i(t) \mathbf{H}_i(\mathbf{x})$$

$\mathbf{x}_i \in \mathbb{R}^d \setminus \bar{\Omega}$ : dipole positions

$\hat{\mathbf{d}}_i \in \mathbb{R}^d$ : field direction



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# Problem 1: Fixed final time

## ► Minimization problem:

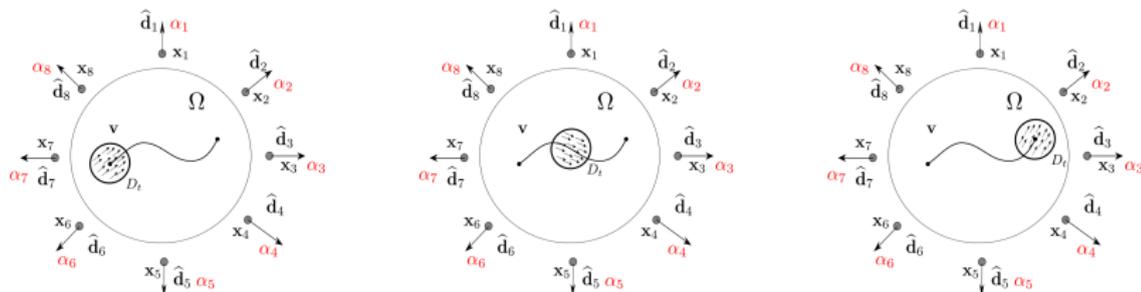
$$\min_{\alpha \in \mathcal{H}_{ad}} \mathcal{J}(\alpha), \quad \text{with } \frac{1}{2} \int_0^T \|\nabla |\mathbf{H}(\alpha)|^2 - \mathbf{f}\|_{L^2(D_t)}^2 dt + \frac{\lambda}{2} \int_0^T |d_t \alpha|^2 dt,$$

with  $\alpha(t) := (\alpha_1(t), \dots, \alpha_{n_p}(t))^T$  in

$$\mathcal{H}_{ad} := \left\{ \alpha \in [H^1(0, T)]^{n_p} : \alpha(0) = \alpha_0 \quad \text{and} \quad \alpha_* \leq \alpha(t) \leq \alpha^*, \quad \forall t \in [0, T] \right\}.$$

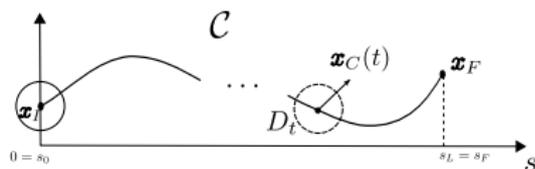
## ► Reformulation:

$$\min_{\alpha \in \mathcal{H}_{ad}} \mathcal{J}(\alpha), \quad \text{with } \mathcal{J}(\alpha) = \frac{1}{2} \int_0^T \left( \sum_{i=1}^d \|\alpha^\top \mathbf{P}_i \alpha - \mathbf{f}_i\|_{L^2(D_t)}^2 + \lambda |d_t \alpha|^2 \right) dt.$$



## Problem 2: Minimizing the final time

- ▶ **Unknown  $f$ .** Since the final time  $T_F$  is an unknown, thus  $f$  is not meaningful quantity. We treat  $f$  as an unknown.
- ▶ Let  $\rho \in C^1[0, s_F]$  be a parameterization of  $\mathcal{C}$  with respect to arc length.



- ▶ Assume that the barycenter  $x_C(t)$  of  $D_t$  moves along curve  $\mathcal{C}$  at speed  $\theta(t) > 0$  with initial position  $x_I$  and final  $x_F$  such that

$$\int_0^{T_F} \theta(\tau) d\tau = s_F.$$

- ▶ We define the map  $\sigma(\cdot) : [0, T_F] \rightarrow [0, s_F]$  as

$$s = \sigma(t) = \int_0^t \theta(\tau) d\tau.$$

- ▶ Whence  $x_C(\cdot) = \rho \circ \sigma(\cdot)$ . Also  $d_t x_C(t) = \theta(t) d_t \rho(\sigma(t))$ .

## Problem 2: Minimizing the final time

$$\min_{(\boldsymbol{\alpha}, \theta) \in \mathcal{H}_{ad} \times \mathcal{V}_{ad}} \mathcal{F}(\boldsymbol{\alpha}, \theta)$$

with

$$\mathcal{F}(\boldsymbol{\alpha}, \theta) := \int_0^{s_F} \left( \frac{1}{2\theta(s)} \sum_{i=1}^d \|\boldsymbol{\alpha}(s)^\top \mathbf{P}_i \boldsymbol{\alpha}(s) - \boldsymbol{\rho}'_i(s)\theta(s)\|_{L^2(D_s)}^2 + \frac{\beta}{\theta(s)} + \frac{\lambda}{2} |d_s \boldsymbol{\alpha}(s)|^2 + \frac{\eta}{2} |d_s \theta(s)|^2 \right) ds$$

and

$$\mathcal{U}_{ad} := \left\{ \boldsymbol{\alpha} \in H^1(0, s_F) : \boldsymbol{\alpha}(0) = \boldsymbol{\alpha}_0 \quad \text{and} \quad \boldsymbol{\alpha}_* \leq \boldsymbol{\alpha}(s) \leq \boldsymbol{\alpha}^*, \quad \forall s \in [0, s_F] \right\},$$
$$\mathcal{V}_{ad} := \left\{ \theta \in H^1(0, s_F) : \theta(0) = \theta_0 \quad \text{and} \quad 0 < \theta_* \leq \theta(s) \leq \theta^*, \quad \forall s \in [0, s_F] \right\}.$$

# Well-posedness of continuous problem

- ▶ **Existence of solution.** If  $\mathbf{f} \in [L^2(0, T; L^2(\Omega))]^d$  then using direct method of calculus of variations, there exist a solution to Problem 1. Same holds for Problem 2 if  $\rho$  is  $C^1$ .
- ▶ **First order necessary optimality conditions.**

- ▶ If  $\bar{\alpha} \in \mathcal{U}_{ad}$  solves Problem 1 then

$$\mathcal{J}'(\bar{\alpha})(\alpha - \bar{\alpha}) \geq 0 \quad \forall \alpha \in \mathcal{H}_{ad}.$$

- ▶ If  $(\bar{\alpha}, \bar{\theta}) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$  solves Problem 2 then

$$\nabla \mathcal{F}(\bar{\alpha}, \bar{\theta})(\delta\alpha, \delta\theta) \geq 0 \quad \forall (\alpha, \theta) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$$

where  $\delta\alpha = \alpha - \bar{\alpha}$ ,  $\delta\theta = \theta - \bar{\theta}$ .

- ▶ **Second order sufficient condition.** Under the assumption

$$\mathcal{J}''(\bar{\alpha})(\delta\alpha)^2 \geq \omega |\delta\alpha|_{H^1(0, T)}^2 \quad \forall \delta\alpha \in \mathcal{A}(\bar{\alpha})$$

where  $\mathcal{A}(\alpha) := \left\{ \mathbf{h} \in H_0^1(0, T) : \alpha + \zeta \mathbf{h} \in \mathcal{H}_{ad}, \zeta > 0 \right\}$  there exists a local unique solution to Problem 1. Same applies to Problem 2.

# Problem 1: Reference domain

- ▶ **Reference domain.** We define a reference domain  $\widehat{D} \subset \mathbb{R}^d$  and a map  $\mathbf{X} : [0, T] \times \widehat{D} \rightarrow \overline{\Omega}$ , such that for all  $t \in [0, T]$

$$\begin{aligned}\mathbf{X}(t, \cdot) : \widehat{D} &\rightarrow \overline{D}_t \\ \widehat{\mathbf{x}} &\rightarrow \mathbf{X}(t, \widehat{\mathbf{x}}) = \boldsymbol{\psi}(t) + \psi(t)\widehat{\mathbf{x}},\end{aligned}$$

$\boldsymbol{\psi} : [0, T] \rightarrow \mathbb{R}^d$ ,  $\psi : [0, T] \rightarrow (0, +\infty)$ , and  $\boldsymbol{\psi}, \psi \in \mathbf{H}^1(0, T)$ . Moreover,  $\widehat{D} = D_0$ .

- ▶ **Reference domain cost.** Then, we rewrite  $\mathcal{J}$  as

$$\mathcal{J}(\boldsymbol{\alpha}) = \frac{1}{2} \sum_{i=1}^d \int_0^T \|\boldsymbol{\alpha}^\top \widehat{\mathbf{P}}_i \boldsymbol{\alpha} - \widehat{\mathbf{f}}_i\|_{L^2(\widehat{D})}^2 + \frac{\lambda}{2} \int_0^T |d_t \boldsymbol{\alpha}|^2 = \mathcal{J}^1(\boldsymbol{\alpha}) + \mathcal{J}^2(\boldsymbol{\alpha})$$

with  $\widehat{\mathbf{P}}_i(t, \widehat{\mathbf{x}}) := \mathbf{P}_i(\mathbf{X}(t, \widehat{\mathbf{x}}))\psi(t)^{d/2}$  and  $\widehat{\mathbf{f}}_i(t, \widehat{\mathbf{x}}) = \mathbf{v}_i(t, \mathbf{X}(t, \widehat{\mathbf{x}}))\psi(t)^{d/2}$ , for  $i = 1, \dots, d$ .

# Problem 1: Time discretization

- ▶ Let us fix  $N \in \mathbb{N}$  and let  $\tau := T/N$  be the time step. Now, for  $n = 1, \dots, N$ , we define  $t^n := n\tau$ ,  $\widehat{\mathbf{P}}_i^n = \widehat{\mathbf{P}}_i(t^n)$  and  $\widehat{\mathbf{f}}_i^n$  to be

$$\widehat{\mathbf{f}}_i^n(\cdot) = \frac{1}{\tau} \int_{t^{n-1}}^{t^n} \widehat{\mathbf{f}}_i(t, \cdot) dt, \quad i = 1, \dots, d,$$

which in turn allows us to incorporate a general  $\mathbf{f}$ .

- ▶ **Time discrete problem:** given the initial condition  $\alpha_0 =: \bar{\alpha}_\tau(0)$ , find  $\bar{\alpha}_\tau \subset \mathcal{H}_{ad}^\tau$  solving

$$\bar{\alpha}_\tau = \underset{\alpha_\tau \in \mathcal{H}_{ad}^\tau}{\operatorname{argmin}} \mathcal{J}_\tau(\alpha_\tau), \quad \mathcal{J}_\tau(\alpha_\tau) = \mathcal{J}_\tau^1(\alpha_\tau) + \mathcal{J}_\tau^2(\alpha_\tau),$$

where

$$\begin{aligned} & \mathcal{J}_\tau^1(\alpha_\tau) + \mathcal{J}_\tau^2(\alpha_\tau) \\ &= \tau \sum_{n=1}^N \frac{1}{2} \sum_{i=1}^d \|(\alpha_\tau^n)^\top \widehat{\mathbf{P}}_i^n \alpha_\tau^n - \widehat{\mathbf{f}}_i^n\|_{L^2(\widehat{D})}^2 + \tau \sum_{n=1}^N \frac{\lambda}{2\tau^2} |\alpha_\tau^n - \alpha_\tau^{n-1}|^2. \end{aligned}$$

and

$$\mathcal{H}_{ad}^\tau := \{\alpha_\tau \in \mathbf{H}^1(0, T) : \alpha_\tau|_{[t^{n-1}, t^n]} \in \mathbb{P}^1, n = 1, \dots, N\} \cap \mathcal{H}_{ad}.$$

# Convergence of scheme

**Theorem.** The family of minimizers  $\{\bar{\alpha}_\tau\}_{\tau>0}$  to the discrete problem is

- ▶ uniformly bounded in  $H^1(0, T)$ .
- ▶ it contains a subsequence that converges weakly to  $\bar{\alpha}$  in  $H^1(0, T)$ .
- ▶  $\lim_{\tau \rightarrow 0} \mathcal{J}_\tau(\bar{\alpha}_\tau) = \mathcal{J}(\bar{\alpha})$ .

**The proof is motivated by  $\Gamma$  convergence.**

# Strong convergence to local minimizers

- ▶ **Auxiliary problem:** For a fixed  $\varepsilon > 0$ , we construct a family  $\{\alpha_\tau^\varepsilon\}_{\tau>0}$  upon solving the minimization problem

$$\alpha_\tau^\varepsilon = \operatorname{argmin}_{\alpha_\tau \in \mathcal{H}_{ad}^{\tau,\varepsilon}} \mathcal{J}_\tau(\alpha_\tau),$$

where  $\mathcal{H}_{ad}^{\tau,\varepsilon} = \left\{ \alpha_\tau \in \mathcal{H}_{ad}^\tau : \|\Pi_\tau \bar{\alpha} - \alpha_\tau\|_{L^2(0,T)} \leq \varepsilon \right\}$ .

- ▶ Next using the second order sufficient condition we show that  $\{\alpha_\tau^\varepsilon\}_{\tau>0}$  forms a local solution to our discrete problem.
- ▶ We conclude by showing that  $\|\alpha_\tau^\varepsilon - \bar{\alpha}\|_{H^1(0,T)} \rightarrow 0$  as  $\tau \rightarrow 0$ .

This approach is inspired by Casas and Troeltzsch '02.

## Problem 2: Discretization

- ▶ We consider the following discrete problem: given an initial condition  $(\alpha_0, \theta_0) =: (\alpha_\kappa(0), \theta_\kappa(0))$  find a solution  $(\alpha_\kappa, \theta_\kappa) \in \mathcal{U}_{ad}^\kappa \times \mathcal{V}_{ad}^\kappa$  to

$$\min_{(\alpha_\kappa, \theta_\kappa) \in \mathcal{U}_{ad}^\kappa \times \mathcal{V}_{ad}^\kappa} \mathcal{F}_\kappa(\alpha_\kappa, \theta_\kappa) := \mathcal{F}_\kappa^1(\alpha_\kappa, \theta_\kappa) + \mathcal{F}_\kappa^2(\theta_\kappa) + \mathcal{F}_\kappa^3(\alpha_\kappa) + \mathcal{F}_\kappa^4(\theta_\kappa)$$

where

$$\mathcal{F}_\kappa^1(\alpha_\kappa, \theta_\kappa) = \sum_{m=1}^M \frac{\kappa}{2\theta_\kappa^m} \sum_{i=1}^d \|(\alpha_\kappa^m)^\top \tilde{\mathbf{P}}_i^m \alpha_\kappa^m - \rho'_i(s^m) \theta_\kappa^m\|_{L^2(\hat{D})}^2$$

$$\mathcal{F}_\kappa^2(\theta_\kappa) = \sum_{m=1}^M \frac{\beta\kappa}{\theta_\kappa^m}, \quad \mathcal{F}_\kappa^3(\alpha_\kappa) = \kappa \sum_{m=1}^M \frac{\lambda}{2\kappa^2} |\alpha_\kappa^m - \alpha_\kappa^{m-1}|^2,$$

$$\mathcal{F}_\kappa^4(\theta_\kappa) = \kappa \sum_{m=1}^M \frac{\eta}{2\kappa^2} |\theta_\kappa^m - \theta_\kappa^{m-1}|^2.$$

- ▶ and admissible sets

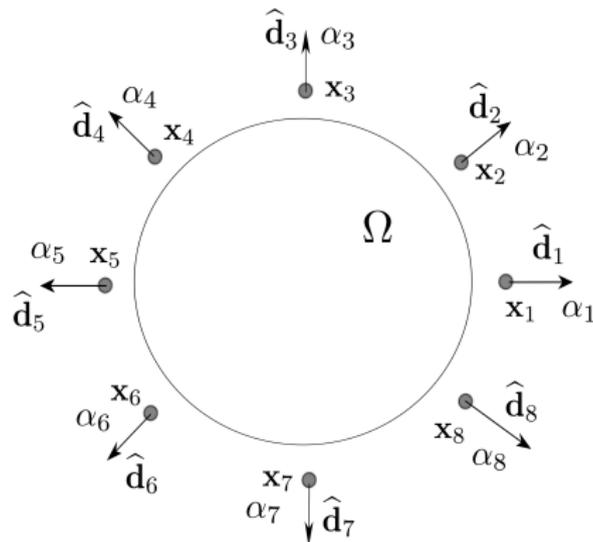
$$\mathcal{U}_{ad}^\kappa := \left\{ \alpha_\kappa \in H^1(0, s_F) : \alpha_\kappa|_{[s^{m-1}, s^m]} \in \mathbb{P}^1, m = 1, \dots, M \right\} \cap \mathcal{U}_{ad},$$

$$\mathcal{V}_{ad}^\kappa := \left\{ \theta_\kappa \in H^1(0, s_F) : \theta_\kappa|_{[s^{m-1}, s^m]} \in \mathbb{P}^1, m = 1, \dots, M \right\} \cap \mathcal{V}_{ad}.$$

- ▶ We again show the weak convergence using  $\Gamma$ -convergence.

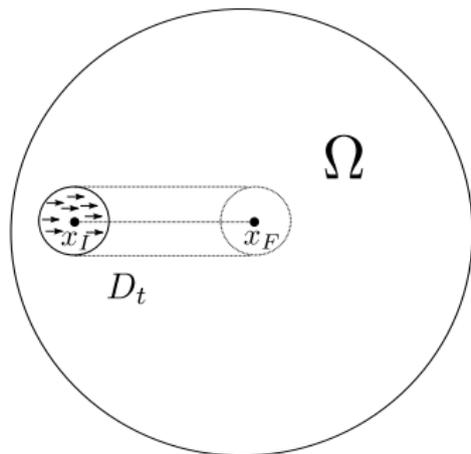
# Numerical examples

- ▶  $\Omega = B_1(0,0) \subset \mathbb{R}^2$ ,  $\widehat{D} = B_{0.2}(-0.75,0)$
- ▶  $\mathbf{x}_{k+1} = 1.2(\cos(k\pi/4), \sin(k\pi/4))$
- ▶  $\widehat{\mathbf{d}}_{k+1} = (\cos(k\pi/4), \sin(k\pi/4)), k = 0, \dots, 7$  ( $n_p = 8$ )

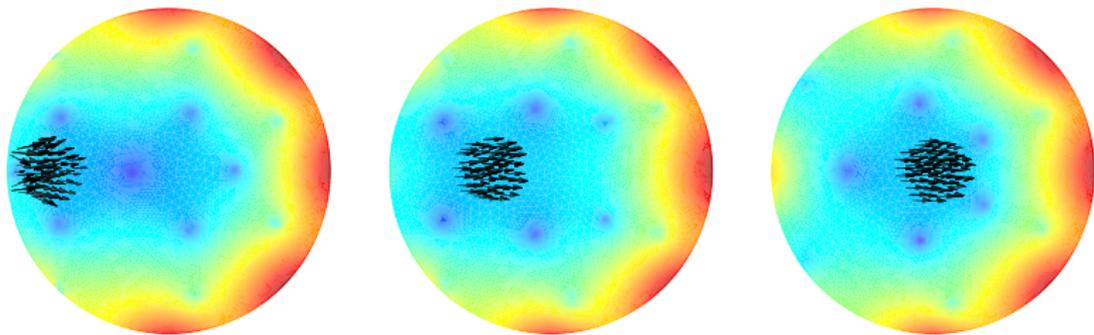


# Problem 1: approximate $\mathbf{f}_1(\mathbf{x}, t) = (1, 0)^\top$

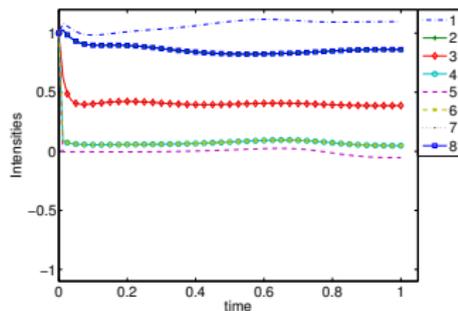
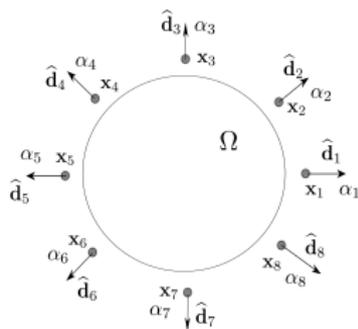
- ▶  $T = 1, \lambda = 10^{-5}$ .
- ▶  $\boldsymbol{\alpha}^* = (2, \dots, 2) \in \mathbb{R}^8$  and  $\boldsymbol{\alpha}_* = (-2, \dots, -2) \in \mathbb{R}^8$ .



Problem 1: approximate  $\mathbf{f}_1(\mathbf{x}, t) = (1, 0)^\top$



Magnetic force at  $t = 0.0125, 0.5$ , and  $1$ .



Dipoles on the left (dipoles 4, 5 and 6) have small intensities at initial times. This is expected because  $D_{1,t}$  is close to the boundary of  $\Omega$ , where  $\mathbf{H}$  is large, thus it is difficult for dipoles 4, 5 and 6 to “push” in the  $\mathbf{f}_1$  direction.

Problem 1: approximate  $\mathbf{f}_1(\mathbf{x}, t) = (1, 0)^\top$

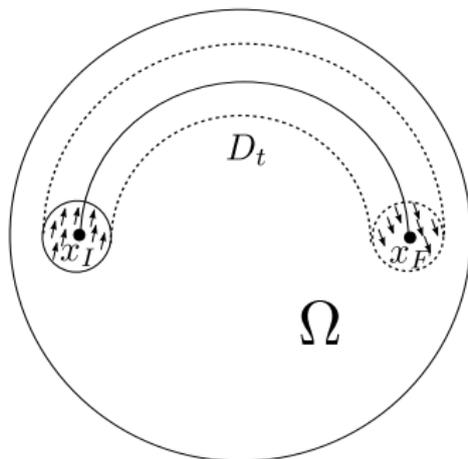
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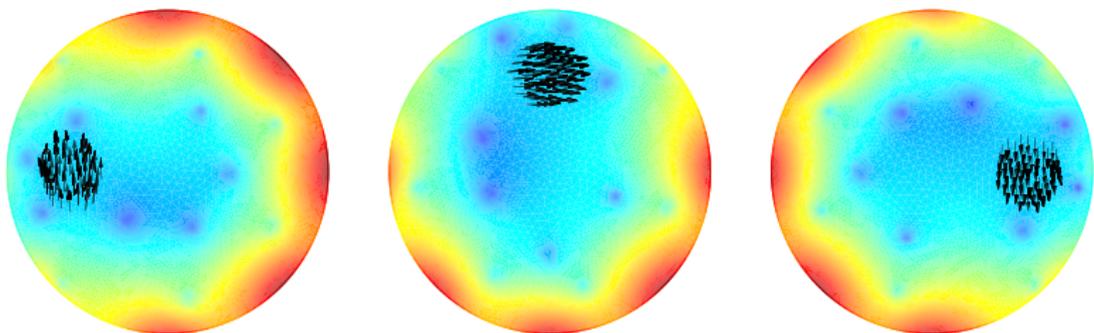
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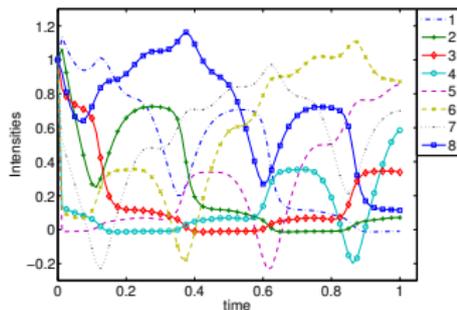
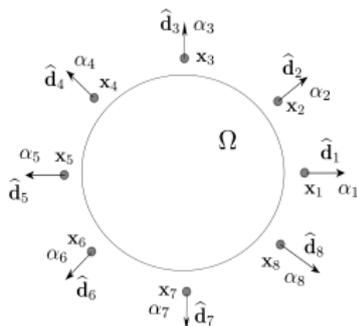
Problem 1: approximate  $\mathbf{f}_2(\mathbf{x}, t) = (\sin(\pi(1 - t)), -\cos(\pi(1 - t)))^\top$



# Problem 1: approximate $\mathbf{f}_2(\mathbf{x}, t) = (\sin(\pi(1 - t)), -\cos(\pi(1 - t)))^\top$



Magnetic force at  $t = 0.015, 0.375$  and  $0.75$ .



Problem 1: approximate  $\mathbf{f}_2(\mathbf{x}, t) = (\sin(\pi(1 - t)), -\cos(\pi(1 - t)))^\top$

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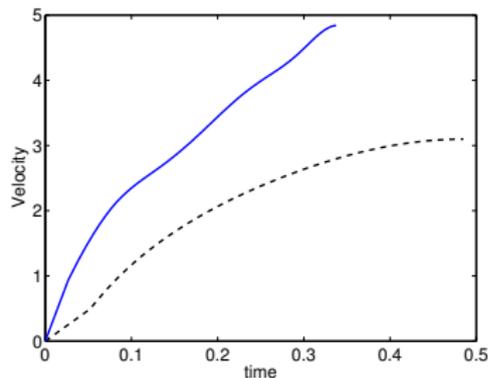
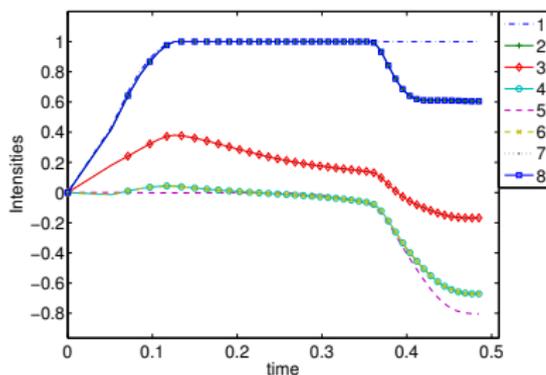
## Problem 2

- ▶ Let the curve  $\mathcal{C}$  is parameterized by

$$\rho(s) = \mathbf{x}_I + s \frac{(\mathbf{x}_F - \mathbf{x}_I)}{\|\mathbf{x}_F - \mathbf{x}_I\|}, \quad s \in [0, 0.75]$$

with  $\mathbf{x}_I = (0, -0.75)$  and  $\mathbf{x}_F = (0, 0)$ .

- ▶  $(\alpha_*, \alpha^*, \theta_*, \theta^*) = (-1, 1, 10^{-10}, 10)$ .
- ▶  $\beta = 10^{-1}$ ,  $\lambda = 10^{-6}$ , and  $\eta = 10^{-4}$ .



# Application: concentration transport

- ▶ **MNPs.** We assume a concentration of magnetic nanoparticles confined in a domain  $\Omega \subset \mathbb{R}^d, d = 2, 3$ .
- ▶ **Drug concentration** is evolved using

$$\begin{aligned}\frac{\partial c}{\partial t} + \operatorname{div}(-A\nabla c + c\mathbf{u} + \gamma_1 cf(\mathbf{H})) &= 0 \quad \text{in } \Omega \times (0, T) \\ c = 0 \quad \text{on } \partial\Omega \times (0, T) \quad c(x, 0) &= c_0 \quad \text{in } \Omega \\ \operatorname{curl} \mathbf{H} = \mathbf{0} \quad \text{in } \Omega \quad \operatorname{div}(\mathbf{H}) &= 0 \quad \text{in } \Omega\end{aligned}$$

where  $A = 10^{-3}$  is a diffusion coefficient matrix,  $\mathbf{u}$  is a fixed velocity vector and  $f$  is the *Kelvin force*.

- ▶ **Goal.** Move  $c_0$  from one subdomain to another (desired location) using the magnetic force  $f$  while minimizing the spreading.

# Application: concentration transport

We solve the parabolic problem with magnetic force given by Problem 1 with  $f_1$ .

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# Conclusions

- ▶ We have approximated a vector field by using the Kelvin force. In particular, we study two problems:
  - ▶ Fixed final time
  - ▶ Unknown final time
- ▶ We prove the existence of solution and using second order sufficient conditions we show the local uniqueness.
- ▶ Motivated by  $\Gamma$ -convergence we show the  $H^1$ -weak convergence of the time-discrete problems.
- ▶ In presence of second order sufficient condition, a  $H^1$ -strong local convergence result is proved for Problem 1.
- ▶ As an application, we study the control of magnetic nanoparticles as those used in magnetic drug delivery. The optimized Kelvin force is used to transport the drug to a desired location.