

# Endovascular Navigation of a Ferromagnetic Microrobot Using MRI-based Predictive Control

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**Abstract**—This paper presents real-time MRI-based control of a ferromagnetic microcapsule for endovascular navigation. The concept was studied for future development of microdevices designed to perform minimally invasive interventions in remote sites accessible through the human cardiovascular system. A system software architecture is presented illustrating the different software modules to allow navigation of a microdevice in blood vessels, namely: (i) vessel path planner, (ii) magnetic gradient steering, (iii) tracking and (iv) closed-loop navigation control. First, the position recognition of the microrobot into the blood vessel is extracted using Frangi vesselness filtering from the pre-operation images. Then, a set of minimal trajectory is predefined, using FMM, to guide the microrobot from the injection point to the tumor area through the anarchic vessel network. Based on the pre-computed path, a GPC is proposed for robust time-multiplexed navigation along a 2D path in presence of pulsative flow. The simulation results suggest the validation of the proposed image processing and control algorithms. A series of disturbances introduced in the presence and absence of closed-loop control affirms the robustness and effectiveness of this predictive control system.

## I. INTRODUCTION

Microrobots designed to perform targeted therapy by navigating in the cardiovascular system are a prolific research area for minimally invasive surgeries [1][2] and treatments efficiency through early diagnosis of diseases [3]. When microrobots are propelled in the body fluids, especially in the blood circulatory system, a very large number of remote locations in the human body become accessible. Nevertheless, as vessels size may vary from 25 mm (aorta) down to 0.010 mm (capillaries), it is obvious that propelling such wireless microdevices within the vessel networks is still a great technical challenge [4]. Because the method of propulsion should allow such a microrobot to navigate through the vascular system, the use of the normal blood flow itself must be considered only as a complementary means of propulsion when the travel path is in the direction of the blood flow. Furthermore, navigation requires observation of the scene in order either to plan the trajectory by off-line mapping, or to correct on-line the microrobot's pose error between the planned and the realized trajectory. Recently, magnetic resonance imaging (MRI)-based medical microrobotic platforms are investigated to reach locations deep in the human body while enhancing targeting efficacy using real-time navigational and trajectory control [5]. For the position recognition of the microrobot in the blood vessels path planning and route optimization

solutions have been proposed. The authors in [6] proposed an endovascular path-planning method based on 3D potential fields and enhanced breath-first search algorithms based on MR-imaging. In [7], Intra-Vascular Ultra-Sound medical imaging technique coupled to pre-operational images of computerized tomography renders possible 3D navigation in blood vessels. Based on these path-planning techniques, only explorative 2D control strategies have been adopted so far using simple proportional-integral-derivative (PID) controller [8]. However, stability and robustness are not ensured against important perturbations (e.g. pulsatile flow whose variations, variation of time-multiplexed sequence...).

The main objective of this paper is to propose an automated technique based on image processing and control algorithms for path finding and navigation control of a ferromagnetic microrobot using a MRI system. The MRI-based control of a ferromagnetic microcapsule presented here is dedicated to convey the microdevice in vessels such as arteries and arterioles. As illustration of the concept, we consider a possible way for the microrobot get into the body through the femoral artery in the leg, which is the normal access point to the circulatory system. One possible application is to locate atherosclerotic lesions in stenosed blood vessels, particularly in vascular circulation, and treat them either chemically or pharmacologically by targeted drug delivery.

The paper is organized as follows. In section II we first present the developed endovascular navigation planning procedure. Then section III-B is devoted to synthesize a predictive control architecture stable and robust against perturbations. Simulation results suggest the validation of the proposed image processing and control algorithms.

## II. ENDOVASCULAR NAVIGATION PLANNING

### A. Finding Endovascular Navigation Path

Finding a navigation path within the vessel network is an essential, primary, and important step which must be addressed prior to the control procedure. The problem of vessels reconstruction has received considerable attention in the computer vision and medical imaging communities [9]. Hence, the literature provide different methods to find a path from a set of medical imaging, such as using tracking-based approaches [5], model-based approaches [10][11], and so on [9]. Most works based on *in vivo* MR-tracking methods usually need many user-defined way points as the input of a controller module for the navigation computation. However, a major drawback remains when the user must define many points manually. Hence, for a complex structure

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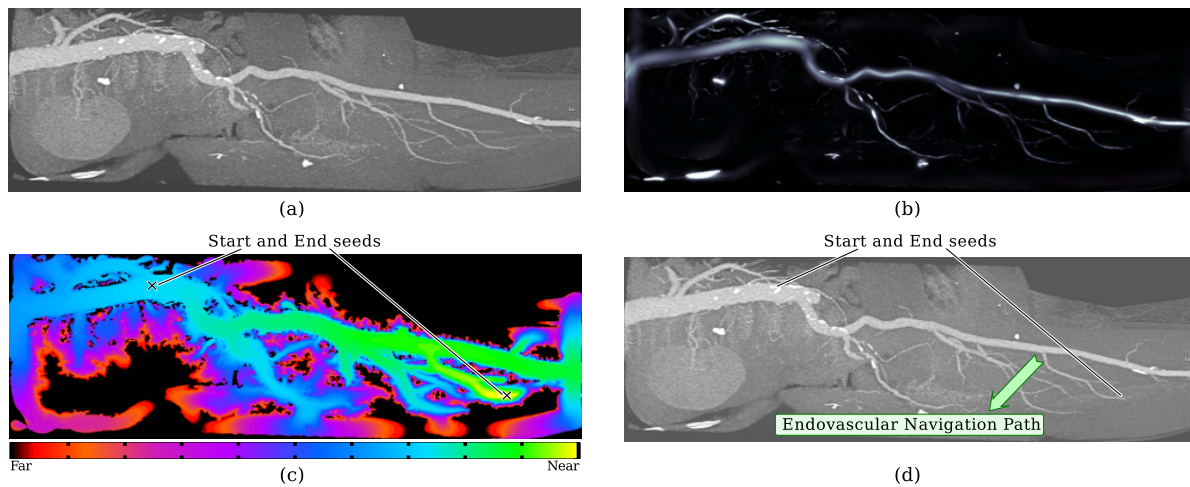


Fig. 1. 2D Navigation path extraction processing of atherosclerotic lesions in the upper right leg: a) Original MRI data; b) Computed cost function using Frangi filter (light pixel have higher weight); c) FFM propagation to build the distance to targeted seed map; d) Extracted navigation path.

(e.g. colon, small vessels...) the required interactivity can be very tedious. Our goal is to focus on the automation of the path construction, reducing the need of interaction and improving performance, in a robust way. Moreover, we need only to find a path from the injection point to the targeted area. To this aim several authors proposed the use of minimum cost path approaches to solve the problem of vessel centerline extraction [10][12][11]. These approaches need at least the start and end point of the vessel, but additional user-interaction can easily be integrated to guide the centerline extraction in difficult cases.

1) *Endovascular Path Extraction*: The path extraction is useful for a range of application domains including medical image analysis, robot navigation, and artificial intelligence. The path extraction technique needs a very simple initialisation and leads to global minimum of a snake-like energy, thus avoiding local minima. Moreover it is fast and accurate. Cohen and Kimmel [13] solved the minimal path problem in 2D with a front propagation equation between the two fixed end points, using the Eikonal equation (that physically models wave-light propagation), with a given initial front. Wink *et al.*[12] explored different methods to determine the minimum cost path through a pre-defined cost image, for extraction of vessel centrelines from medical image data. Early, Sethian [14] explore the use of Fast Marching Method (FMM) to extract minimal paths. This method relies on the fact that the gradient of the FMM arrival function has only one local minimum, with is guaranteed to be global minimum [10]. Therefore the minimal path can be extracted by back-propagating from given the end point of the desired path to the starting point implicitly embedded in the arrival function.

2) *Applications and Navigation Path Extraction Results*: The FMM algorithm, introduced by Sethian [14] is applied here to extract a targeted navigation path within the vessel network. From the set of MRI data we have first to compute a speed map, which must enhance the relevant endovascular network. Choosing an appropriate and efficient image cost function is the most difficult part of the entire process.

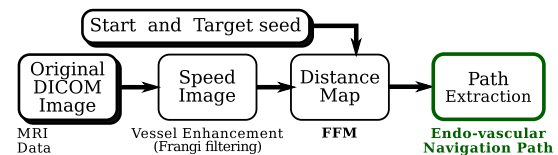


Fig. 2. Image processing pipeline.

We describe in the sequel presented in Fig. 2, the process used to extract navigation path. First, we need a relevant cost function which allow to enhance vessel in the image. To this aim we use some *a priori* knowledge about vessel shape and intensity in MRI data (cf. Fig. 1). Vessels are expected to appear as bright tubular structures in a darker environment. One way to account for the varying size of vessels is by multiscale analysis. It allows us to detect structures of different sizes according to the scale at which they give maximal response. In this context, a typical speed image is produced by using a Frangi vesselness filter [15] which uses the eigenvectors of the Hessian matrix at each pixels of the image to compute the likeliness of an image region to vessels. This mapping is selected in such a way that vessels regions will have higher speed. Once the speed map is generated, the user has to select a start and end seed points in the viewer of the input original image. The FFM will then propagate a front from the start seed and traveling to the targeted area, thanks to the speed map. This step allow to build an image of distance between the start seed and all other pixels. The corresponding shortest path is then traced thanks to the distance map.

In this work, the application is to locate atherosclerotic lesions in stenosed blood vessels, particularly in vascular circulation. Hence, we consider that the microrobot get into the body through the femoral artery in the leg, and treat them pharmacologically, by targeted drug delivery. Fig. 1 shows the different steps to extract a 2D navigation path in the upper right leg.

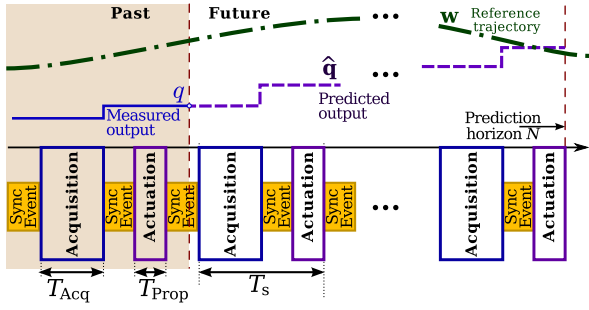


Fig. 3. Timeline of acquisition and control prediction.

### III. MRI-BASED CONTROL DESIGN

#### A. Problem formulation

Endovascular navigation requires observation of the scene in order either to plan the trajectory by off-line mapping, or to correct online the microcapsule's pose error between the planned and the observed trajectory. To insure a smooth conveyance of the microrobot to destination, collisions and the risk to be trapped by the endothelium, optimal navigation performance will be affected by external perturbations and MRI technological constraints (e.g. nonnegligible pulsatile flow, limitations on the MRI duty cycle, limitations on the magnetic gradient amplitude...).

#### B. Real-Time Sequence Design

The overall concept of the in-vivo MRI-tracking system is based on the fact that both tracking and propulsion is possible with the gradient coils of the MRI system. At any instant only one of the functions could be applied (i.e. either tracking or propulsion), but both will be executed over the same MRI platform. The MRI interface has therefore to be shared and a time-division-multiple-access scheme for it has to be developed. Fig. 3 shows an overview of the real-time sequence with time-multiplexed positioning and propulsion phases introduced in [5]. The main relevant aspect to the controller's performance is (i) the duty cycle  $T_{Prop}/T_s$  that stands for the ratio between the propulsion time and the time between two successive position requests, and (ii) the synchronization event delay  $T_{Sync}$  that stands for the minimum time allowed for image processing and real-time control feedback. First, the duty cycle should be adapted to apply sufficient magnetic propulsion gradients during a pre-defined propulsion time  $T_{Prop}$  to prevent the microrobot from drifting away from the trajectory. Second, a large time delay  $T_{Sync}$  produces oscillations as the microrobot approaches the reference trajectory leading to position instabilities. Such limitations have been pointed out in [8] when implementing simple proportional-integral-derivative (PID) controller. We proposed to use a GPC including microrobot's motion and dynamics. A predictive trajectory-tracking control consider a prediction window. The propulsion phase starts during  $T_{Prop}$  seconds at the same initial condition as the prediction phase, recording the performance of the system according to a prediction horizon. After this phase the system ends after a imaging-propulsion sequence at a final position  $q$  which

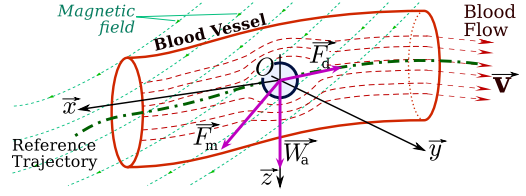


Fig. 4. Forces applied on microrobot navigating in blood vessel.

is set as the new initial condition of the next prediction output  $\hat{q}$ . The proposed GPC offers stability by design [16] and allows the designer to trade-off performance for (computation) speed and stability.

#### C. Model description

The linear model that was used in this work, derived from the nonlinear model developed in a previous study [17]. In [17], we used this model to combine the backstepping controller and high gain observer in order to control the trajectory of microrobot inside a vessel using the MRI gradients, as shown on Fig. 5.

The different forces acting on the microrobot are (see Fig. 4): drag force  $\vec{F}_d$ , apparent weight  $\vec{W}_a$  and magnetic force  $\vec{F}_m$ . The application of Newton's third law and the projection on the  $\vec{x}$ -axis and  $\vec{y}$ -axis leads to:

$$\begin{cases} m\ddot{x} = \vec{F}_{dx} + \vec{F}_{mx} \\ m\ddot{y} = \vec{F}_{dy} + \vec{F}_{my} + \vec{W}_a \end{cases} \quad (1)$$

where  $m$  is the mass of the microrobot.

Let  $\vec{v} = (v_x, v_y)$  denotes the blood flow velocity, and  $(x, y)$  the robot location in the blood vessel wrt. to a given frame  $\mathcal{F}(O, \vec{x}, \vec{y})$ . Taking the drag coefficient  $C_d = \frac{24}{Re}$ , the linear model can be written as follow:

$$\begin{cases} \ddot{x} = \alpha_1 (\dot{x} - v_x) + \alpha_2 u_x \\ \ddot{y} = \beta_1 (\dot{y} - v_y) + \beta_2 u_y \end{cases} \quad (2)$$

where the magnetic gradients is considered as control inputs  $u_x$  and  $u_y$ , and the parameters  $\alpha_i$  and  $\beta_i$  is given by:

$$\begin{cases} \alpha_1 = -4.5 \frac{\eta \cos \theta}{r^2 \rho}, & u_x = \left\| \vec{\nabla} B_x \right\| \\ \beta_1 = -4.5 \frac{\eta \sin \theta}{r^2 \rho}, & u_y = \left\| \vec{\nabla} B_y \right\| \\ \alpha_2 = \beta_2 = \frac{M}{\rho} \end{cases} \quad (3)$$

where  $\rho = 8 \text{ g/cm}^3$  is the density of the microdevice;  $\eta = 15 \text{ mPa} \cdot \text{s}$  is the fluid viscosity;  $r = 300 \text{ } \mu\text{m}$  is the spherical radius of the microrobot;  $M = 1.95 \cdot 10^6 \text{ A/m}$  denotes the magnetization of the core; and  $\mathbf{B} = (B_x, B_y)^T$  is the magnetic field generate by the MRI system.

Finally, the state-space representation is deduce from (2):

$$(S) \begin{cases} \dot{x} = v_x \\ \dot{v}_x = \alpha_1 v_x - \alpha_1 v_{fx} + \alpha_2 u_x \\ \dot{y} = v_y \\ \dot{v}_y = \beta_1 v_y - \beta_1 v_{fy} + \beta_2 u_y \\ q = (x, y)^T \end{cases} \quad (S_x) \quad (S_y) \quad (4)$$

where  $(v_x, v_y)^T$  denote the robot velocity along  $\vec{x}$ -axis and  $\vec{y}$ -axis. We can notice that system (S) can be divided into

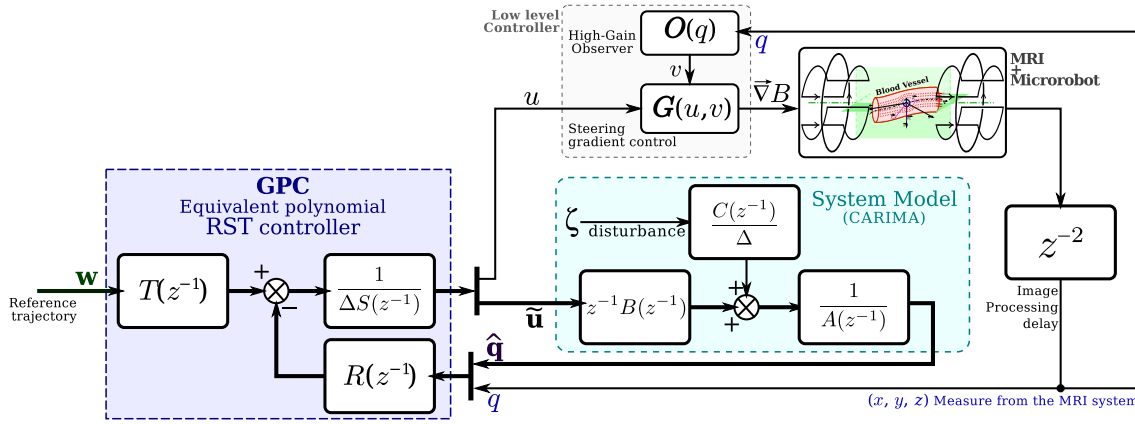


Fig. 5. Generalized Predictive Control (GPC) strategy of a ferromagnetic microrobot using MRI system.

two subsystems ( $S_x$ ) and ( $S_y$ ), which allow us to define two independent GPC schemes to track the reference trajectory in 2D MRI data.

In this paper we aim to embed the system model (4) in high level a GPC scheme in order to follow efficiently a pre-planned path extracted with the method proposed in section II-A. Our controller is intended to be above our low level robust controller designed in [17] (see Fig. 5).

#### D. Generalized Predictive Control (GPC)

Generalized Predictive Control (GPC) belongs to the class of Model Predictive Control (MPC) techniques and was first introduced by Clarck *et al.*[18]. GPC approach is a popular control predictive method, experienced on several applications, especially in industrial process [19]. It combines the prediction of future behavior of the system with feedback control (see Fig. 5). A process model is explicitly used to predict the future behavior of the system over the given time horizon. From this prediction, a control is computed by minimizing a quadratic cost function.

1) *GPC Scheme Design:* The system is modeled using the model Controlled Auto-Regressive Integrated Moving-Average (CARIMA) with integrator form, that is [18]:

$$A(z^{-1})q(t) = B(z^{-1})u(t-1) + C(z^{-1})\frac{\zeta(t)}{\Delta(z^{-1})}, \quad (5)$$

where  $\Delta(z^{-1}) = 1 - z^{-1}$  define the difference operator;  $\zeta(t)$  is a zero mean white noise; and  $A(z^{-1})$ ,  $B(z^{-1})$  and  $C(z^{-1})$  are polynomial matrix in the backward shift operator  $z^{-1}$ .

The GPC is classically obtained by minimizing a weighted sum of square predicted future errors and square control signal increments:

$$J_{\{N_1, N_2, N_u, \lambda\}} = \sum_{j=N_1}^{N_2} (\hat{y}(t+j) - w(t+j))^2 + \lambda \sum_{j=1}^{N_u} \Delta u^2(t+j-1) \quad (6)$$

where  $\hat{y}(t+j)$  is the optimum predicted output of the system at time  $t+j$ ;  $w(t+j)$  is the future reference;  $N_1$  and  $N_2$  are the minimum and the maximum of the prediction horizon;  $N_u$  is the control horizon; and  $\lambda > 0$  is the control weighting.

Classically a RST polynomial structure is introduced at the end to determine a relation between the output  $q(t)$ , the control signal  $u(t)$  and the reference  $w(t)$  (see Fig. 5). The advantage of RST structure is that these modules can be computed off-line, providing a very short real-time loop and on the other hand offers the possibility to analyze the stability of the controlled open loop in the frequency domain. In fact, this off-line operation is a very helpful strategy to determine the stable set of tuning parameters just before applying the control law on the real system.

2) *GPC implementation:* In order to design the GPC controller the transfer functions of the two subsystems ( $S_x$ ) and ( $S_y$ ) are computed from their state-space representation (4), and its given by:

$$H_{S_x}(s) = \frac{243.8}{s^2 + 49.25s}, \quad \text{and} \quad H_{S_y}(s) = \frac{243.8}{s^2 + 79.77s} \quad (7)$$

To ensure good stability, our GPC scheme under RST polynomial form requires tuning of the set parameters  $\{N_1, N_2, N_u, \lambda_x, \lambda_y\}$ , where  $\lambda_x$  and  $\lambda_y$  are the control increment weighting for the two subsystems ( $S_x$ ) and ( $S_y$ ) respectively. Some guidelines may be found in the literature [16]. Thus, two independent GPC controller have to be designed for the system sampling period  $T_s = 50$  ms. For instance, we consider the following tuning parameters, which satisfy stability and robustness features [16]:

$$\{N_1 = 1; N_2 = 4; N_u = 1; \lambda_x = 0.77; \lambda_y = 0.34\} \quad (8)$$

According to these parameters, the model of the process using (7) in CARIMA (5) form is written as follow:

$$\begin{cases} A_{S_x}(z^{-1}) &= [1 - 1.085z^{-1} + 0.085z^{-2}] \\ B_{S_x}(z^{-1}) &= [0.155 + 0.071z^{-1}] \end{cases}, \quad (9)$$

$$\begin{cases} A_{S_y}(z^{-1}) &= [1 - 1.018z^{-1} + 0.018z^{-2}] \\ B_{S_y}(z^{-1}) &= [0.115 + 0.034z^{-1}] \end{cases}, \quad (10)$$

and where  $C_{S_x}(z^{-1})$  and  $C_{S_y}(z^{-1})$  are set to 1. The RST form optimal control is:

$$\Delta u_x^{\text{Opt}}(t) S_x(z^{-1}) = T_x(z^{-1}) w_x(t) - R_x(z^{-1}) q_x(t) \quad (11)$$

$$\Delta u_y^{\text{Opt}}(t) S_y(z^{-1}) = T_y(z^{-1}) w_y(t) - R_y(z^{-1}) q_y(t) \quad (12)$$



with:

$$\begin{cases} R_x(z^{-1}) &= 2.855 - 2.222z^{-1} + 0.169z^{-2} \\ S_x(z^{-1}) &= 1 + 0.140z^{-1} \\ T_x(z^{-1}) &= 0.123z + 0.273z^2 + 0.405z^3 \end{cases} \quad (13)$$

$$\begin{cases} R_y(z^{-1}) &= 4.061 - 2.906z^{-1} + 0.052z^{-2} \\ S_y(z^{-1}) &= 1 + 0.098z^{-1} \\ T_y(z^{-1}) &= 0.206z + 0.410z^2 + 0.592z^3 \end{cases} \quad (14)$$

### E. Results

Different situations are considered in this section to illustrate and validate the performance and robustness of the proposed MRI-based predictive controller shown on Fig. 5. As the considered system is decoupled into two subsystems ( $S_x$ ) and ( $S_y$ ) (4), we have first validate the control strategy onto 1D longitudinal path. As illustration, the microrobot has to follow a sinusoidal reference trajectory (cf. Fig. 6 and 7) for different time horizons  $N = N_2 - N_1$ .

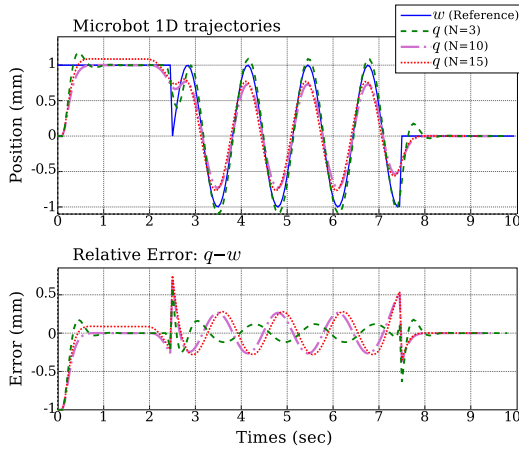


Fig. 6. Longitudinal position microrobot control.

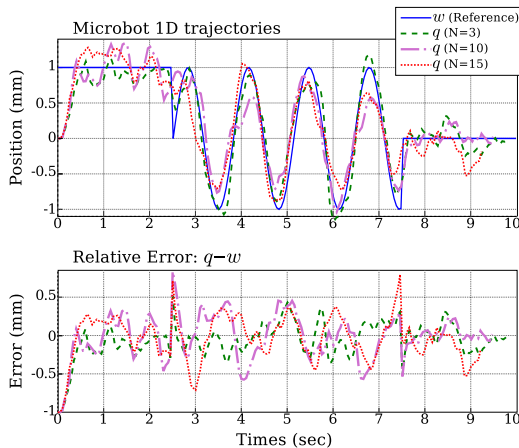


Fig. 7. Longitudinal position microrobot control with white noise.

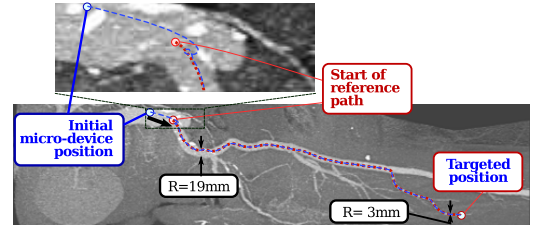
Fig. 6 presents the trajectories followed by the microrobot, and the relative error between the current position  $q$  and the reference  $w$ . As one can see the system output follows correctly the reference trajectory  $w$  for each considered prediction horizon  $N$ . The output of the closed loop system

is dependent on the setting parameters of the GPC. The previous curves show the impact of  $N$  on the system. Moreover, comparing the different plots, the nature of anticipation of the GPC scheme is illustrate: greater is  $N$  more is anticipate the path behavior. Hence, a great value of  $N$  does not necessarily guarantee good performance, and classically increase the complexity of the scheme.

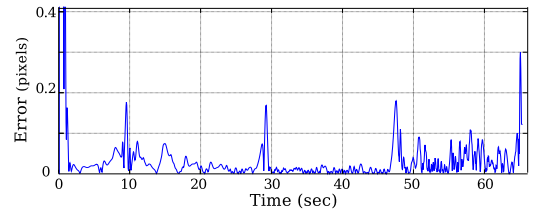
To evaluate the efficiency of the proposed MRI-based predictive controller, we added a white Gaussian noise on the system output measure  $q$ . Fig. 7 shows the system response in the presence of this disturbance on the system. Globally, tracking is not too much affected by the noise, since position standard deviation (std) and root mean square (RMS) error are quite satisfactory (see table I).

TABLE I  
ERROR STATISTICS

	1D with noise (mm)			2D navigation (pixels)	
	$N = 3$	$N = 10$	$N = 15$	without noise	with noise
std	0.2303	0.2971	0.2949	1.0438	1.2121
RMS	0.2368	0.2967	0.2959	1.0480	1.2306



(a) 2D trajecrories without noise.

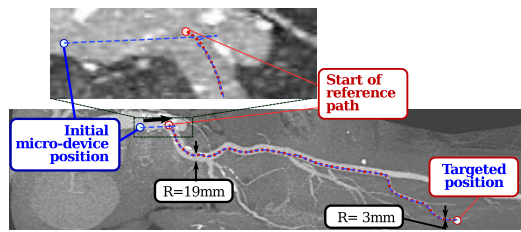


(b) Tracking error ( $N = 3$ ):  $\|q - w\|$

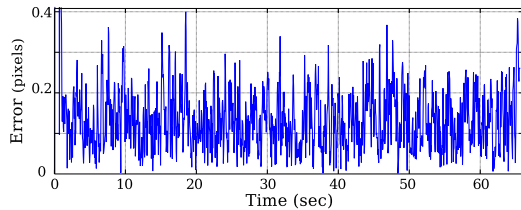
Fig. 8. 2D MRI-based microrobot endovascular navigation ( $N = 3$ ).

We validated the proposed control strategy on 2D endovascular navigation path extracted from MRI-data with the method presented in section II-A. As shown in Fig. 8 and 9, the system output  $q$  follows perfectly the reference trajectory  $w$ , either without or with white Gaussian noise added. In particular, the microrobot are able to reach quickly the navigation path, in spite of a big gap between the initial position  $q$  and the begin of reference  $w$  (about 50 pixels). Fig. 8(b) and 9(b) describe the error evolution in both cases. Once again the error remains small with low values of std and RMS parameters. Let us notice that these 2D error statistics given in table I take into account the gap between the initial microrobot position and the start of the reference path.

Finally, to evaluate the robustness of our strategy, we have performed some tests in which some model parameters (4) are not well identified, and the white noise still added. As



(a) 2D trajectories with white noise.



(b) Tracking error:  $\|q - w\|$

Fig. 9. 2D endovascular navigation ( $N = 3$ ) with a white noise.

illustrated in Fig. 10, the 2D trajectory tracking error is quite important, but still remains satisfactory.

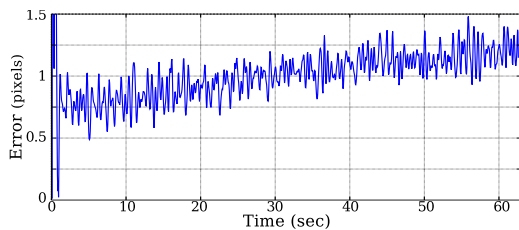


Fig. 10. 2D trajectory tracking error  $\|q - w\|$ , with noise and wrong model parameters ( $r + 30\%$  and  $\eta + 10\%$ )

#### IV. CONCLUSIONS

We have proposed a planning and controlling strategies for a ferromagnetic microdevice using a MRI system. Planning have been realized thanks to a FMM path extraction procedure which is computationally efficient and provide a minimal path with very few user interaction. The microcapsule position control strategy has been developed at milliscala and microscale, where a GPC have been designed. The proposed control architecture (with a low and high controller) allow to ensure robustness against pulsatile flow and time-multiplexing variation. The main drawback of MRI-based navigation stems from the strong limitations on the magnetic gradient amplitude of available MRI devices. As magnetic forces used for propelling are volumetric, whereas the drag force is at best dependent on the microcapsule's area, the smaller the capsule, the higher the required control forces with respect to hydrodynamic perturbations. Consequently, this approach is well conditioned for beads whose radius is up to a few dozen micrometers with actual MRI devices. Targeting aims at focusing these microcarriers and stopping them through embolization at the arterioles entry close to the occluded blood vessels. Possible releasing mechanisms could rely on biodegradable polymer and techniques used

in hyperthermia where aggregates of nanocapsules can be heated to melt polymer. Such a solution is actually under experimentation for validation of the proposed minimally invasive MRI-based microrobotic system.

#### V. ACKNOWLEDGMENTS

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