

DETERMINING THE DISTRIBUTION OF ION CHANNELS FROM EXPERIMENTAL DATA [☆]

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Abstract. The authors study an integral inverse problem arising in the biology of the olfactory system. The transduction of an odor into an electrical signal is accomplished by a depolarising influx of ions through cyclic-nucleotide-gated (CNG for short) channels on the cilium membrane. The inverse problem studied in this paper consists in finding the spatial distribution of the CNG channels from the measured transduce electrical signals. The Mellin transform allows us to write an explicit formula for its solution. Proving observability and continuity inequalities is then a question of estimating the Mellin transform of the kernel of this integral equation on vertical lines. New estimates using arguments in the spirit of the stationary phase method are proven and a numerical scheme is proposed to reconstruct the density of CNG channels from modeled current representing experimental data, for an approximated model. For the original model an identifiability and a non observability (in some weighted L^2 spaces) results are proven.

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1. INTRODUCTION

1.1. Olfactory transduction *via* inverse modelling

Identification of detailed features of neuronal systems is a major issue in the biosciences for the coming years. In this respect, inverse problem methods and models have already shown not only to be efficient but also to have given answers to relevant questions regarding the transduction of chemical information into an electrical signal [5, 11, 12]. As a contribution to this field, this paper proposes and analyses a new mathematical model to determine the spatial distribution of CNG ion channels along the length of a cilium. It corresponds to a new approach for a simplified model developed by D.A. French *et al.* in [11]. We present both theoretical

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and numerical results, which are contrasted with modeled current representing experimental data obtained by French in [10].

Cilia are long thin cylindrical structures that extend from an olfactory receptor into the nasal mucus. When an odorant molecule binds to an olfactory receptor in a cilium membrane, it successively activates two enzymes, which results in an increase in the concentration of cyclic adenosine monophosphate (cAMP) concentration within the olfactory receptor neuron. Some of the cAMP binds to cyclic nucleotide-gated (CNG) ion channels, causing them to open. This allows a depolarizing influx of Na^+ ions to flow into the cell, which causes the neuron to depolarize. More details about this biological mechanism can be found in the textbook [7] (Part five, 16, II), for instance. Although the single-channel properties have been well described, the distribution of these channels along the cilia remains still widely unknown and may well turn out to be crucial in determining the kinetics of the neuronal response.

Experimental procedures to isolate a single (grass frog) cilium have been developed in [8, 12, 14, 15, 16]. One olfactory cilium is drawn into a pipette which is then moved to a pseudo intracellular bath which contains no cAMP. The pipette containing the cilium is then transferred to a bath containing cAMP. Contact with the bath initiates the diffusion of cAMP into the cilium. The transmembrane electrical current through the cilium is recorded.

A very natural issue is whether it is possible to determine the CNG channel distribution along the length of a cilium from transmembrane experimental current data. In [11] the authors proposed a mathematical model for the dynamics of cAMP concentration in this experiment, consisting of two nonlinear differential equations and a constrained Fredholm integral equation of the first kind. Numerical methods to compute the channel distribution were proposed in [9, 11]. However, specific computations indicated that this mathematical problem is highly ill-conditioned.

To determine mathematically the CNG channels distribution along the cilium, some simplifications proposed in [10] and resulted in the inverse problem of determining a function, say $\rho = \rho(x) \geq 0$, representing the distribution of the CNG channels, from measurements in time of the transmembrane electrical current, denoted $I_0[\rho]$. This mathematical model for ρ is an integral equation of the following form:

$$\forall t \geq 0 \quad I_0[\rho](t) := \int_0^L \rho(x) H_0(c(t, x)) dx, \quad (1.1)$$

where H_0 is known as the Hill function of exponent $n > 0$. It is defined by:

$$\forall c \geq 0 \quad H_0(c) := \frac{c^n}{c^n + K_{1/2}^n}. \quad (1.2)$$

In this definition, the parameter n represents the average number of bound molecules when a CNG ion channel opens, while $K_{1/2} > 0$ represents the half-bulk concentration. These parameters are experimentally determined. On the other hand, in the integral equation (1.1), $c(t, x)$ denotes the concentration of cAMP. This ligand diffuses along the cilium with a diffusivity constant D . In (1.1), L denotes the length of the cilium, which, for simplicity, is assumed to be one-dimensional.

Hill type functions are extensively used in biochemistry to model the fraction of ligand bound to a macromolecule as a function of the ligand concentration. Since the presence of cAMP on the cilium membrane triggers the opening of the CNG channels, in equation (1.1), the quantity $H_0(c(t, x))$ models the fraction of opened CNG channel as a function of the cAMP concentration. In others words, $H_0(c(t, x))$ can be regarded as the probability of opening of a CNG channel as a function of the cAMP concentration; see [13] for more details. After [5, 10],

we assume that $c(t, x)$ is known, analytically, and given by:

$$c(t, x) := c_0 \operatorname{erfc} \left(\frac{x}{2\sqrt{Dt}} \right), \tag{1.3}$$

where $c_0 > 0$ is the maintained concentration of cAMP with which the pipette comes into contact at the open end ($x = 0$) of the cilium (while $x = L$ is the closed end). Here, $\operatorname{erfc} := 1 - \operatorname{erf}$ and erf is the Gauss error function:

$$\operatorname{erf}(z) := 2\pi^{-1/2} \int_0^z e^{-\tau^2} d\tau.$$

Accordingly, it is straightforward to check that c is decreasing in both its variables and that it remains bounded: for all (t, x) , $0 \leq c(t, x) \leq c_0$.

Despite its elegance, thanks to the simplicity of its formulation, the model (1.1) to recover ρ from $I_0[\rho]$ does not overcome the unsatisfactory issues found in its non-linear version, it still leads to several theoretical and practical difficulties due to the fact that this problem is ill-posed, mathematically. Indeed, since $H_0(c(t, x))$ is a smooth mapping, the operator $\rho \mapsto I_0[\rho]$ is compact from $L^p(0, L)$ to $L^p(0, T)$ for every $L, T > 0$, $1 < p < \infty$. Thus, even if the operator I_0 would be injective, its inverse would not be continuous, because if so, then the identity map in $L^p(0, L)$ would be compact, which is knowingly false.

As already mentioned, the quantity $H_0(c(t, x))$ in (1.2) is a typical choice in biochemical contexts. However, from a purely mathematical viewpoint, it is clear, from the proofs contained in this paper, that any model based on a first-order integral equation which has a diffusive and smooth kernel, gives rise to an ill-posed inverse problem. Thus, an approximation of $H_0(c(t, x))$ by a non-diffusive and non-smooth kernel seems to be inevitable when proposing a mathematical model for this biochemical process.

A natural way to overcome this ill-posedness of the model (1.1) consists of replacing the kernel of the integral equation with a non-smooth variant of the Hill function. Precisely, let $a \in (0, c_0)$ be a given real parameter. The new kernel we consider is obtained by keeping the original Hill function H_0 in the interval $[0, a]$, and by forcing a saturation state for higher concentrations. Thereby, we are led to introduce the following disruptive version of H_0 (see Fig. 1):

$$H_1(c) := H_0(c) \mathbb{1}_{c \leq a} + \mathbb{1}_{a < c \leq c_0}, \tag{1.4}$$

where $\mathbb{1}_J$ denotes the characteristic function of the interval J . Based on (1.4), we are now in a position of proposing an inverse mathematical model to recover the distribution of the CNG channels ρ from the measured transmembrane electrical current, which is now modeled by the integral operator:

$$I_1[\rho](t) := \int_0^L \rho(x) H_1(c(t, x)) dx, \tag{1.5}$$

where $c(t, x)$ is still defined by (1.3). From a mathematical viewpoint the approximation made can be understood by the fact, as t tends to $+\infty$, the factor x/\sqrt{Dt} appearing in (1.3) tends to 0, and consequently $c(t, x)$ tends to c_0 .

1.2. Main results

The main aim of this paper is to study model (1.5). We consider the direct problem and associated inverse problems. We prove identifiability and observability results, as well as continuity/stability with respect to measured data. Since (1.5) is a Fredholm equation of the first type, it is natural to tackle it using the convolution

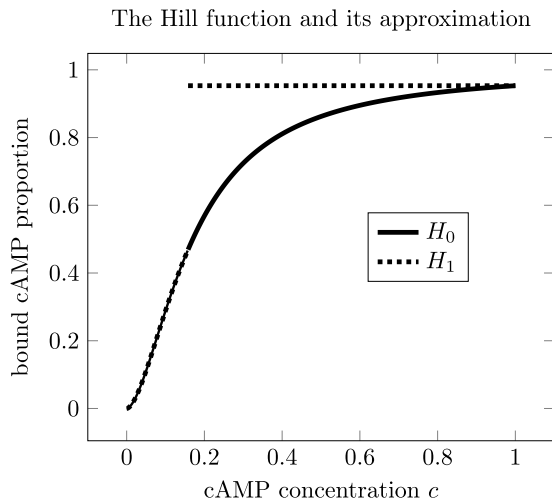


FIGURE 1. The Hill function H_0 , defined by (1.2), and its disruptive version H_1 (dashed line) defined by (1.4), for $a = 0.157$.

formalism. The convolution is of multiplicative type and the Mellin transform¹ is the most appropriate tool to carry out this task. In particular, we prove that problem (1.5) admits a unique solution in a weighted L^2 space, and that it depends continuously on the first derivative $(I_1[\rho])'$ of the corresponding measured current. Moreover, this method allows us to reconstruct the CNG channels distribution ρ from the modeled experimental data, using numerical simulations.

More precisely, let us introduce the following notations regarding weighted Banach spaces. For q in \mathbb{R} , $q + i\mathbb{R}$ denotes the vertical line $\{q + it, t \in \mathbb{R}\}$ of the complex plane having abscissa q , and for $p \in \mathbb{R}$ ($p \geq 1$), $L^p([0, \infty), x^q)$, or simply L^p_q , stands for the Lebesgue space with the weight x^q , *i.e.*,

$$L^p_q = \left\{ f : [0, \infty) \rightarrow \mathbb{R} \mid \|f\|_{L^p_q} < +\infty \right\},$$

where

$$\|f\|_{L^p_q} = \left(\int_0^\infty |f(x)|^p x^q dx \right)^{1/p}.$$

The space L^p_q endowed with this norm is a Banach space.

As we shall see, integral operator (1.5) can be written in terms of a multiplicative convolution. Thus our problem comes down to a deconvolution problem. We refer the reader to [19] and the references therein, for an introduction to this subject. A classical tool to tackle a deconvolution problem is the Fourier transform. It changes an additive convolution into a pointwise product of Fourier transforms. In this paper we use the Mellin transform, which changes a multiplicative convolution into a pointwise product of Mellin transforms. The sought for inequalities of stability and observability for model (1.5) is reduced to find lower and upper bounds in L^p_q spaces for the Mellin transform of suitable functions involving $H_1(c(t, x))$. This study allows us to determine the unique ion channels distribution from measurements of the transmembrane electric current. More precisely, we prove the following theorem.

¹Hjalmar Mellin (1854–1933), see [18] for a summary of his works, gave his name to the so-called Mellin transform, which definition and some properties are recalled in Section 2.

Theorem 1.1 (Existence and uniqueness of ρ). *Let $a > 0$ and $r < 1$ be given. If $I_1 \in L^2_{(r-3)/2}$, $I'_1 \in L^2_{2+(r-3)/2}$ and a has a small enough value, then there exists a unique $\rho \in L^2_r$ which satisfies the following stability condition:*

$$\|I_1\|_{L^2_{(r-3)/2}} + \|(I_1)'\|_{L^2_{2+(r-3)/2}} \geq C \|\rho\|_{L^2_r},$$

where $C > 0$ depends only on a and r .

It is worth mentioning that since the original model (1.1) is also a Fredholm integral equation of the first kind, it is natural to apply here, also, the Mellin transform. By doing this, interesting negative results can be derived: neither an observability inequality nor a numerical reconstruction algorithm for ρ can be established. However, an identifiability result holds true if the transmembrane electric current is measured over an open time interval (see Prop. 4.11). More precisely, we establish the following result.

Proposition 1.2. *Let $r < 0$ and $\rho \in L^1_r$. We consider the operator $I_0[\rho]$ defined by (1.1), (1.2), (1.3). If there exists a non empty open set U of $(0, \infty)$ such that:*

$$\forall t \in U \quad I_0[\rho](t) = 0,$$

then $\rho = 0$ a.e. on $(0, \infty)$.

1.3. Complementary results

Another natural way to tackle the ill-posedness of problem (1.1) was developed in [5]. Exploiting the fact that the Hill function converges pointwise to a single step function as the exponent n goes to $+\infty$, the method used in [5] was to approximate H_0 by a multiple step function. Precisely, let $0 < \alpha_1 < \alpha_2 < \dots < \alpha_m < c_0$ be a sequence of real points and $(a_k)_{1 \leq k \leq m}$ be m positive weights such that $\sum_{j=1}^m a_j = 1$. Then, an approximate transmembrane electrical current is introduced through the integral equation:

$$I_2[\rho](t) := \int_0^L \rho(x) H_2(c(t, x)) dx, \tag{1.6}$$

where the kernel H_2 is defined as:

$$H_2(c) := \sum_{j=1}^m a_j \mathbb{1}_{c \geq \alpha_j}. \tag{1.7}$$

Based in different assumptions on the spaces where the unknown ρ is sought, identifiability, stability and reconstruction results were obtained using other than Mellin transform techniques. In this paper, we also revisit, very briefly, an inverse problem associated to (1.6) under the perspective of the Mellin transform. Doing this, we are able to improve the observability result obtained in [5] and recover the continuity of the solution with respect to experimental data on the transduce electrical signal. Exactly, in Section 4 we prove Proposition 4.2, which can be anticipated as follows.

Proposition 1.3. *Let $I_2[\rho]$ be defined by (1.3), (1.7), (1.6). Suitable hypotheses on r imply the following results.*

- *There exist constants $C, C' > 0$ such that, for every ρ in L^2_r , we have:*

$$\|I_2[\rho]\|_{L^2_{(r-3)/2}} \leq C \|\rho\|_{L^2_r}, \quad \text{and} \quad \|(I_2[\rho])'\|_{L^2_{(r+1)/2}} \leq C' \|\rho\|_{L^2_r}. \tag{1.8}$$

- There exists a constant $C > 0$ such that, for every $(I_2[\rho])'$ in $L^2_{(r+1)/2}$, we have:

$$\|(I_2[\rho])'\|_{L^2_{(r+1)/2}} \geq C \|\rho\|_{L^2_r}. \tag{1.9}$$

1.4. Outline

The paper is organized as follows. Section 2 presents some definitions and results concerning the Mellin transform. Section 3 introduces the main idea for using the Mellin transform to invert the integral operators I_0, I_1, I_2 . In Section 4, continuity and observability inequalities are stated and proved. For two different approximations of the Hill function we obtain positive results and for the original Hill function we obtain an identifiability result and a non observability result. The proof of the technical Lemma 4.10 is postponed up to Appendix A. Section 5 presents some numerical simulations illustrating the theoretical results of Section 4, and other simulations performed with modeled experimental data.

2. THE MELLIN TRANSFORM

The construction of the Mellin transform on $i\mathbb{R}$ can be done in the general context of the Fourier transform on a locally compact abelian group, we refer the reader to chapter 1 of [20]. Here we consider the *multiplicative* abelian group $G = (0, \infty)$ (with unit 1), equipped with the topology inherited from \mathbb{R} and with the *Haar measure* $\frac{dx}{x}$ (that is the unique measure on G , up to a positive multiplicative constant, which is translation-invariant). It is easy to show that the dual group Γ of all the characters of G with the Gelfand topology is isomorphic to $i\mathbb{R}$ with the topology inherited from \mathbb{C} via $i\mathbb{R} \rightarrow \Gamma \quad it \mapsto (x \mapsto x^{-it})$. In this general context the L^1 and L^2 theories can be built, with the same results, as the Fourier transform on the topological group $(\mathbb{R}^n, +, dx)$. The extension of the Mellin transform to a vertical strip $q + i\mathbb{R}$ of the complex plane \mathbb{C} is obtained by defining $\mathcal{M}f(q + it) = \mathcal{M}g(it)$ with $g(x) = x^q f(x)$.

Notation 2.1 (Pochhammer symbol). For a real number x and a non-negative integer n we write: $(x)_0 = 1$ and $(x)_n = x \cdots (x - n + 1) = \prod_{j=0}^{n-1} (x - j)$ for $n \geq 1$.

Throughout this paper we also assume that the nullary product is one. For instance: $\forall q \in \mathbb{R}, k \in \mathbb{N} \quad (x^q)^{(k)} = (q)_k x^{q-k}$.

Notation 2.2. For a function $f : q + i\mathbb{R} \rightarrow \mathbb{C}$ we denote $\|f\|_{L^p(q+i\mathbb{R})} = (\int_{\mathbb{R}} |f(q + it)|^p dt)^{1/p}$. We also denote $L^p(q + i\mathbb{R})$ the Banach space $L^p(q + i\mathbb{R}, dx)$ with the norm $\|\cdot\|_{L^p(q+i\mathbb{R})}$.

Definition 2.3. Let f be in L^1_q . The Mellin transform of f is a complex valued function defined on the vertical line $q + 1 + i\mathbb{R}$ by:

$$\mathcal{M}f(s) := \int_0^\infty x^s f(x) \frac{dx}{x}.$$

Theorem 2.4 (Riemann-Lebesgue). The Mellin transform is a linear continuous map of L^1_q into $C^0(q + 1 + i\mathbb{R}) \subset L^\infty(q + 1 + i\mathbb{R})$, its operator norm is 1.

Proposition 2.5. If f is in L^1_q for every real number q in (a, b) then its Mellin transform $\mathcal{M}f$ is holomorphic in the strip $S = \{s \in \mathbb{C} \mid a + 1 < \text{Re } s < b + 1\}$.

Proposition 2.6.

Function	Mellin transform
$f(at), a > 0$	$a^{-s} \mathcal{M}f(s)$
$f(t^a), a \neq 0$	$ a ^{-1} \mathcal{M}f(a^{-1}s)$
$f^{(k)}(t)$	$(-1)^k (s-k)_k \mathcal{M}f(s-k)$

Examples.

- For $\operatorname{erfc}(z) = 2\pi^{-1/2} \int_z^{+\infty} \exp(-t^2) dt$, one obtains, after integrating by parts, for $\operatorname{Re} s > 0$:

$$\mathcal{M} \operatorname{erfc}(s) = \frac{1}{\sqrt{\pi s}} \Gamma\left(\frac{s+1}{2}\right).$$

- If H_0 is the Hill function, then $1 - H_0(x) = f(K_{1/2}^{-n} x^n)$ with $f(x) = \frac{1}{1+x}$. Using that $\mathcal{M}f(s) = \frac{\pi}{\sin(\pi s)}$ for $0 < \operatorname{Re} s < 1$ and Proposition 2.6, one obtains, for $0 < \operatorname{Re} s < n$:

$$\mathcal{M}(1 - H_0)(s) = K_{1/2}^s \frac{1}{n} \mathcal{M}f\left(\frac{s}{n}\right) = \frac{\pi}{n} \frac{K_{1/2}^s}{\sin \frac{\pi s}{n}}.$$

Theorem 2.7 (Inversion Theorem). *If f is in L^1_q and if $\|\mathcal{M}f\|_{L^1(q+i\mathbb{R})}$ is finite, then one can define*

$$\mathcal{M}_q^{-1} f(x) = (2\pi)^{-1} \int_{\mathbb{R}} f(q+it) x^{-(q+it)} dt.$$

The Inversion Theorem states that:

$$f = \mathcal{M}_{q+1}^{-1}(\mathcal{M}f) \quad \text{a.e. in } (0, \infty).$$

Definition 2.8. For two functions f, g we define the *multiplicative convolution* $f * g$ by:

$$(f * g)(x) = \int_0^\infty f(y) g\left(\frac{x}{y}\right) \frac{dy}{y}.$$

Proposition 2.9.

$$\mathcal{M}(f * g)(s) = \mathcal{M}f(s) \mathcal{M}g(s),$$

whenever this expression is well defined.

Proposition 2.10. *For a function f in $L^1_{q-1} \cap L^2_{2q-1}$, we have:*

$$\|f\|_{L^2_{2q-1}} = (2\pi)^{-1/2} \|\mathcal{M}f\|_{L^2(q+i\mathbb{R})}.$$

As the subspace $L^1_{q-1} \cap L^2_{2q-1}$ is dense in L^2_{2q-1} this identity allows us to extend the Mellin transform to L^2_{2q-1} .

Theorem 2.11 (Plancherel Transform). *According to the previous formula the Mellin transform can be extended, in a unique manner, to an isometry (up to the multiplicative constant $(2\pi)^{-1/2}$) of L^2_{2q-1} onto $L^2(q+i\mathbb{R})$.*

3. APPLICATION OF THE MELLIN TRANSFORM

In this section we use Mellin transform to study an integral equation of the same type as the three equations considered in the introduction, namely (1.1), (1.5), (1.6). Since all results are valid for all three models, we momentarily unify the notation and simply write H for H_l , $l = 0, 1$, or 2 , and $I[\rho]$ the corresponding transmembrane electrical current. Thus in this section we focus on the following generic equation:

$$\forall t \geq 0 \quad I[\rho](t) = \int_0^L \rho(x) H(c(t, x)) \, dx, \tag{3.1}$$

where $c(t, x)$ is still defined by (1.3). One key observation is that the kernel $H(c(t, x))$ in (3.1) can be written as a function of $z = \frac{\sqrt{t}}{x}$. Indeed, let us introduce functions G and J defined by:

$$G(z) := H(c_0 \operatorname{erfc}(2^{-1} D^{-1/2} z^{-1})) \quad \text{and} \quad J(y) := H(c_0 \operatorname{erfc}(y)). \tag{3.2}$$

Then (3.1) can be rewritten as follows:

$$\forall t \geq 0 \quad I[\rho](t) = \int_0^L \rho(x) G\left(\frac{\sqrt{t}}{x}\right) \, dx. \tag{3.3}$$

As we see right away, this latter expression allows us to rewrite the integral equation (3.1) as a multiplicative convolution equation with respect to the Mellin transform. But to achieve this, it is necessary to change the time scale t to t^2 and the unknown $\rho(x)$ to $x\rho(x)$. Precisely, by virtue of Definition 2.8, the following formal identity holds:

$$I[\rho](t^2) = \int_0^\infty x\rho(x) \mathbb{1}_{x \in [0, L]} G\left(\frac{t}{x}\right) \frac{dx}{x} = \left(x\rho(x) \mathbb{1}_{x \in [0, L]}\right) * G, \tag{3.4}$$

where $*$ is the multiplicative convolution. For the sake of simplicity, in all the sequel, we denote $\rho(x) = \rho(x) \mathbb{1}_{x \in [0, L]}$, *i.e.* the function ρ is extended by 0 on $[L, \infty)$.

Taking the Mellin transform of this identity we obtain:

$$\begin{aligned} \mathcal{M}G(s)\mathcal{M}\rho(s+1) &= \mathcal{M}G(s) \mathcal{M}(x\rho(x))(s) \\ &= \mathcal{M}(I[\rho](t^2))(s) = \frac{1}{2} \mathcal{M}I[\rho](s/2). \end{aligned} \tag{3.5}$$

Proposition 2.6 shows that the functions G and J and their Mellin transforms are linked by the following relations:

$$G(x) = J(2^{-1} D^{-1/2} x^{-1}) \quad \text{and} \quad \mathcal{M}G(s) = 2^{-s} D^{-s/2} \mathcal{M}J(-s). \tag{3.6}$$

Thus, we obtain, formally

$$\mathcal{M}\rho(s+1) = 2^{s-1} D^{s/2} \frac{\mathcal{M}I[\rho](s/2)}{\mathcal{M}J(-s)}. \tag{3.7}$$

Therefore, finding continuity or observability inequalities for the operator $I[\rho]$ is reduced to bounding $\mathcal{M}J(s)$ from above or from below respectively, on the vertical line on which the inverse Mellin transform is taken. The following lemma makes this link precise.

Lemma 3.1. *Let $k \in \mathbb{N}, r \in \mathbb{R}$ and let us consider the operators I, G, J defined by (3.3), (3.2). We have the following bounds:*

$$C_l \|\rho\|_{L^2_r} \leq \left\| (I[\rho])^{(k)} \right\|_{L^2_{2k + \frac{r-3}{2}}} \leq C_u \|\rho\|_{L^2_r}, \tag{3.8}$$

where

$$C_l = 2^{1/2} \inf_{s \in \frac{r-1}{2} + i\mathbb{R}} \left| \left(\frac{s}{2} \right)_k \mathcal{M}G(s) \right|, \quad C_u = 2^{1/2} \sup_{s \in \frac{r-1}{2} + i\mathbb{R}} \left| \left(\frac{s}{2} \right)_k \mathcal{M}G(s) \right|,$$

do not depend on ρ in L^2_r .

It is worth noting that C_u and C_l can range from 0 to $+\infty$.

Proof of Lemma 3.1. The proof consists in taking the equation (3.5), making computations in the Mellin variables, and coming back to the real variables, using twice the isometry induced by the Mellin transform on L^2 spaces, see Theorem 2.11.

The equality (3.5) leads to:

$$\begin{aligned} \mathcal{M}I[\rho](s) &= 2 \mathcal{M}G(2s) \mathcal{M}\rho(2s + 1) \\ (s - k)_k \mathcal{M}I[\rho](s - k) &= 2(s - k)_k \mathcal{M}G(2(s - k)) \mathcal{M}\rho(2(s - k) + 1). \end{aligned} \tag{3.9}$$

As the Mellin transform is an isometry (up to the factor $(2\pi)^{-1/2}$) of L^2_{2q-1} onto $L^2(q + i\mathbb{R})$ (see Thrm. 2.11), for s in $q + i\mathbb{R}$ the previous relation (3.9) yields:

$$\begin{aligned} \left\| (I[\rho])^{(k)} \right\|_{L^2_{2q-1}} &= (2\pi)^{-1/2} \left\| (-1)^k (s - k)_k \mathcal{M}I[\rho](s - k) \right\|_{L^2(q+i\mathbb{R})} \\ &= 2 (2\pi)^{-1/2} \left\| (s - k)_k \mathcal{M}G(2(s - k)) \mathcal{M}\rho(2(s - k) + 1) \right\|_{L^2(q+i\mathbb{R})} \\ &= 2 (2\pi)^{-1/2} \left\| (s)_k \mathcal{M}G(2s) \mathcal{M}\rho(2s + 1) \right\|_{L^2(q-k+i\mathbb{R})} \\ &= 2 (2\pi)^{-1/2} 2^{-1/2} \left\| \left(\frac{s}{2} \right)_k \mathcal{M}G(s) \mathcal{M}\rho(s + 1) \right\|_{L^2(2(q-k)+i\mathbb{R})}. \end{aligned} \tag{3.10}$$

As \mathcal{M} is an isometry of $L^2(2(q - k) + 1 + i\mathbb{R})$ onto $L^2_{4(q-k)+1}$, we have:

$$\|\mathcal{M}\rho(s + 1)\|_{L^2(2(q-k)+i\mathbb{R})} = \|\mathcal{M}\rho(s)\|_{L^2(2(q-k)+1+i\mathbb{R})} = (2\pi)^{1/2} \|\rho\|_{L^2_{4(q-k)+1}}. \tag{3.11}$$

Thanks to (3.10), (3.11) and the definitions of C_l, C_u , we obtain:

$$C_l \|\rho\|_{L^2_{4(q-k)+1}} \leq \left\| (I[\rho])^{(k)} \right\|_{L^2_{2q-1}} \leq C_u \|\rho\|_{L^2_{4(q-k)+1}}.$$

Taking $r = 4(q - k) + 1$, that is $q = k + \frac{r-1}{4}$, provides the result. □

Lemma 3.2. *Let $k \in \mathbb{N}, r \in \mathbb{R}$ and let us consider the operators I, G, J defined by (3.3), (3.2). We have the following results:*

a) Assume that there exists a constant $C > 0$ such that:

$$\left| \prod_{j=0}^{k-1} (s + 2j) \mathcal{M}J(s) \right| \leq C \quad \text{on } \frac{1-r}{2} + i\mathbb{R}.$$

Then, there exists a constant \widetilde{C}_u , such that, for every ρ in L_r^2 , we have:

$$\left\| (\mathbb{I}[\rho])^{(k)} \right\|_{L^2_{2k + \frac{r-3}{2}}} \leq \widetilde{C}_u \|\rho\|_{L_r^2}.$$

b) For the reverse inequality, assume that there exists a constant $C > 0$ such that:

$$\left| \prod_{j=0}^{k-1} (s + 2j) \mathcal{M}J(s) \right| \geq C \quad \text{on } \frac{1-r}{2} + i\mathbb{R}.$$

Then there exists a constant \widetilde{C}_l , such that, for every ρ in L_r^2 , we have:

$$\left\| (\mathbb{I}[\rho])^{(k)} \right\|_{L^2_{2k + \frac{r-3}{2}}} \geq \widetilde{C}_l \|\rho\|_{L_r^2}.$$

Proof. It is a direct consequence of Lemma 3.1, rewriting the constants C_l, C_u appearing in this lemma in terms of $\left| \prod_{j=0}^{k-1} (s + 2j) \mathcal{M}J(s) \right|$.

Using the relation between $\mathcal{M}G$ and $\mathcal{M}J$ given by (3.6), we have:

$$\begin{aligned} C_l &= 2^{1/2} \inf_{s \in \frac{r-1}{2} + i\mathbb{R}} \left| \left(\frac{s}{2}\right)_k \mathcal{M}G(s) \right| = 2^{1/2} \inf_{s \in \frac{r-1}{2} + i\mathbb{R}} \left| \left(\frac{s}{2}\right)_k 2^{-s} D^{-s/2} \mathcal{M}J(-s) \right| \\ &= 2^{1-r/2} D^{(1-r)/4} \inf_{s \in \frac{r-1}{2} + i\mathbb{R}} \left| \left(\frac{s}{2}\right)_k \mathcal{M}J(-s) \right| = 2^{1-r/2} D^{(1-r)/4} \inf_{s \in \frac{1-r}{2} + i\mathbb{R}} \left| \left(\frac{-s}{2}\right)_k \mathcal{M}J(s) \right|. \end{aligned} \tag{3.12}$$

The functions J_0 and J_1 , defined by (1.2), (1.4), (3.2), are shown in Figure 2. As:

$$\left(\frac{-s}{2}\right)_k = \prod_{j=0}^{k-1} \left(-\frac{s}{2} - j\right) = (-1)^k 2^{-k} \prod_{j=0}^{k-1} (s + 2j),$$

we obtain:

$$C_l = 2^{1-k-r/2} D^{(1-r)/4} \inf_{s \in \frac{1-r}{2} + i\mathbb{R}} \left| \prod_{j=0}^{k-1} (s + 2j) \mathcal{M}J(s) \right|,$$

This concludes the proof taking $\widetilde{C}_l = 2^{1-k-r/2} D^{(1-r)/4} C$. The proof is analogous for the upper bound \widetilde{C}_u . □

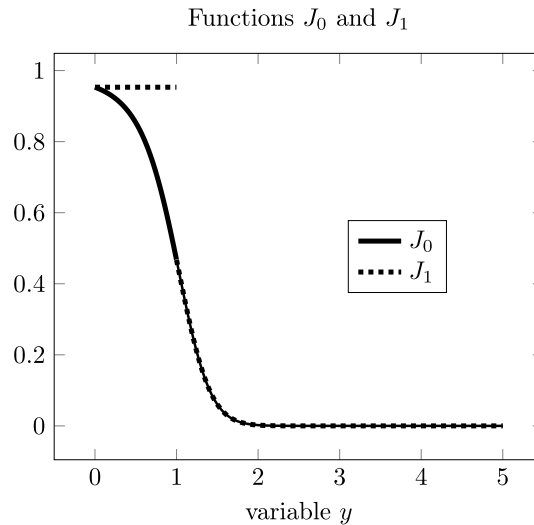


FIGURE 2. The function J_0 , defined by (1.2), (3.2), and its disruptive version J_1 (dashed line) defined by (1.4), (3.2), for $a = 0.157$.

As a consequence of formula (3.7) and of Lemma 3.2, the strategy to prove continuity/observability results for the operators I , in a weighted L^2 space, is to find an integer power $k \in \mathbb{N}$ such that $|s^k \mathcal{M}J(s)|$ is bounded from above/below on a vertical line, whose abscissa depends on the weight of the L^2 space.

4. PROOFS OF THE MAIN RESULTS

This section is devoted to the application of the results of Section 3 to each particular case in which the kernel H is either H_1 , H_2 or H_0 . To do so, it is worth noticing that for the current operators I_1 and I_2 the integer k appearing in Lemma 3.2 can be taken to be 1 (see Lem. 4.1 and Cor. 4.5), whereas for the original current operator I_0 , $\mathcal{M}J_0(s)$ decays faster than any power function s^k (see Lems. 4.9 and 4.10). The converse of Lemma 3.2 is true and implies that no observability inequality of the previous type holds for the original operator I_0 . We now state the results for each case.

First, let us consider the approximation $I_2[\rho]$ of the operator $I_0[\rho]$. In this case the Mellin transform $\mathcal{M}J_2$ can be computed explicitly and Lemma 4.1 provides explicit bounds. To do so let us define:

$$\beta_j = \operatorname{erfc}^{-1} \left(\frac{\alpha_j}{c_0} \right), \tag{4.1}$$

where the numbers a_j, α_j were defined in (1.7).

Lemma 4.1. *Let the β_k 's be defined by (4.1), (1.7) and let J_2 be defined by (1.7), (3.2). For $s = q + it$ with $q > 0$, the Mellin transform of J_2 is given by:*

$$\mathcal{M}J_2(s) = \frac{1}{s} \sum_{j=1}^m a_j \beta_j^s.$$

And there exists q_1 with $q_1 \geq 0$, such that:

$$\forall q > q_1 \exists C > 0 \forall s \in q + i\mathbb{R} : |s\mathcal{M}J_2(s)| \geq C.$$

Proof of Lemma 4.1. As erfc is a decreasing function, we have:

$$J_2(x) = H_2(c_0 \operatorname{erfc}(x)) = \sum_{j=1}^m a_j \mathbb{1}_{c_0 \operatorname{erfc}(x) \geq \alpha_j} = \sum_{j=1}^m a_j \mathbb{1}_{x \leq \beta_j}.$$

The explicit formula for $\mathcal{M}J_2$ is then a consequence of the linearity of \mathcal{M} and of:

$$\mathcal{M}(\mathbb{1}_{0 \leq x \leq a})(s) = \frac{1}{s} a^s \quad \text{for } \operatorname{Re} s > 0.$$

As $a_j > 0$ and $0 < \alpha_1 < \dots < \alpha_m < c_0$, the β_k 's are decreasing, i.e. $0 < \beta_m < \dots < \beta_1 < \infty$. Given $q > 0$, we have:

$$\left| \sum_{j=1}^m a_j \beta_j^{q+it} \right| \geq a_1 \beta_1^q - \sum_{j=2}^m a_j \beta_j^q \geq \beta_1^q \left(a_1 - \left(\frac{\beta_2}{\beta_1} \right)^q \sum_{j=2}^m a_j \right).$$

Thus we can take:

$$q_1 = \max \left\{ \frac{\ln(a_1) - \ln(\sum_{j=2}^m a_j)}{\ln(\beta_2) - \ln(\beta_1)}, 0 \right\}.$$

Therefore, we get that $|s\mathcal{M}J_2(s)|$ is bounded from below when $q > q_1$. □

Lemma 4.1 allows us to establish Proposition 4.2.

Proposition 4.2. *Let $I_2[\rho]$ be defined by (1.3), (1.7), (1.6).*

- Let $r < 1$. There exist constants $C, C' > 0$ such that, for every ρ in L_r^2 , we have:

$$\|I_2[\rho]\|_{L_{\frac{r-3}{2}}^2} \leq C \|\rho\|_{L_r^2} \quad \text{and} \quad \|(I_2[\rho])'\|_{L_{\frac{r+1}{2}}^2} \leq C' \|\rho\|_{L_r^2}. \tag{4.2}$$

- Let q_1 given by Lemma 4.1 and let $r < 1 - 2q_1$. There exists a constant $C > 0$ such that, for every $(I_2[\rho])'$ in $L_{\frac{r+1}{2}}^2$, we have:

$$\|(I_2[\rho])'\|_{L_{\frac{r+1}{2}}^2} \geq C \|\rho\|_{L_r^2}. \tag{4.3}$$

Proof of Proposition 4.2.

- Let $q > 0, s \in q + i\mathbb{R}$, for $k = 0$ or 1 . The explicit formula of Lemma 4.1 implies that:

$$|s^k \mathcal{M}J_2(s)| \leq |s|^{k-1} \sum_{j=1}^m a_j \beta_j^q \leq C |s|^{k-1} \leq C. \tag{4.4}$$

Now let $r < 1$, that is $q = \frac{1-r}{2} > 0$. Using (4.4) and applying Lemma 3.2 for $k = 0, 1$ on the vertical line $\frac{1-r}{2} + i\mathbb{R}$ leads to the continuity inequalities (4.2).

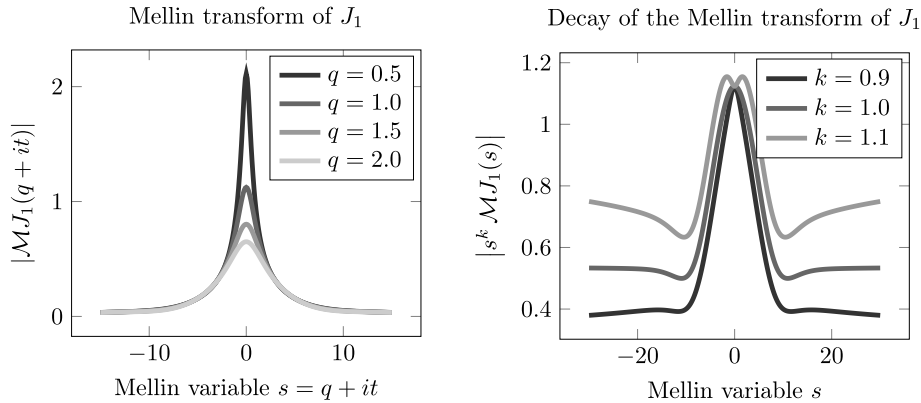


FIGURE 3. The Mellin transform $|\mathcal{M}J_1(s)|$, with $s = q + it$, for some values of q (left panel) and $|s^k \mathcal{M}J_1(s)|$, for some values of k (right panel), for $s \in 1 + i\mathbb{R}$, $a = 0.1573$, $K = \frac{c_0^n}{K_{1/2}^n + c_0^n}$. For small values of a the function $|s^k \mathcal{M}J_1(s)|$ is bounded from below for $k \geq 1$, see Proposition 4.3 and Corollary 4.5.

- Let $q > q_1$, with $s \in q + i\mathbb{R}$, $k \geq 1$. The explicit formula of Lemma 4.1 leads to the following bounds:

$$|s^k \mathcal{M}J_2(s)| \geq |s|^{k-1} \beta_1^q \left(a_1 - \left(\frac{\beta_2}{\beta_1} \right)^q \sum_{j=2}^m a_j \right) \geq C > 0.$$

Now let $r < 1 - 2q_1$, that is $\frac{1-r}{2} > q_1$. Applying Lemma 3.2 for $k = 1$ on the vertical line $\frac{1-r}{2} + i\mathbb{R}$ we obtain (4.3). □

Second, let us consider the non linear approximation $I_1[\rho]$ of the operator $I_0[\rho]$. In this case the computations are no longer explicit. Nevertheless an argument in the spirit of the stationary phase method proves that $\mathcal{M}J_1(s)$ has the same behavior as $\mathcal{M}J_2(s)$, if the real number a involved in the definition of H_1 has a small enough value. This is illustrated in Figure 3. This idea allows us to establish Proposition 4.3.

Proposition 4.3. *Let $a > 0$ and $I_1[\rho]$ be defined by (1.3), (1.4), (1.5). Let $r < 1$.*

- *There exists a constant $C > 0$ such that, for every ρ in L_r^2 , we have:*

$$\|I_1[\rho]\|_{L_{\frac{r-3}{2}}^2} \leq C \|\rho\|_{L_r^2}.$$

- *If a has a small enough value, then there exists a constant $C > 0$ such that, for every ρ in L_r^2 , we have:*

$$\|(I_1[\rho])'\|_{L_{\frac{r+1}{2}}^2} \leq C' \|\rho\|_{L_r^2}.$$

- *If a has a small enough value, then there exists a constant $C > 0$ such that, for every $(I_1[\rho])'$ in $L_{\frac{r+1}{2}}^2$, we have:*

$$\|(I_1[\rho])'\|_{L_{\frac{r+1}{2}}^2} \geq C \|\rho\|_{L_r^2}.$$

The proof of Proposition 4.3 is based on two technical lemmas.

Lemma 4.4. *Let A and B be two elements of $[0, \infty]$, $k \in \mathbb{N}$ an integer and f a function such that $f^{(j)}$ is in $L^1_j(A, B)$ for every $j = 0, \dots, k$. For every real number t , we have:*

$$\int_A^B f(x)x^{it} dx = \sum_{j=0}^{k-1} (-1)^j Q_j(t) \left[x^{j+1} f^{(j)}(x)x^{it} \right]_A^B + (-1)^k Q_{k-1}(t) \int_A^B x^k f^{(k)}(x)x^{it} dx,$$

where $Q_j(t) = \left(\prod_{l=0}^j (1 + l + it) \right)^{-1}$.

Proof. The proof is by induction on $k \in \mathbb{N}$. For $k = 0$, using $Q_{-1} = 1$, there is nothing to prove. We assume that the formula is true for an integer $k \in \mathbb{N}$. As $(k + 1 + it)Q_k = Q_{k-1}$ it remains to be proved that:

$$(k + 1 + it) \int_A^B x^k f^{(k)}(x)x^{it} dx = \left[x^{k+1} f^{(k)}(x)x^{it} \right]_A^B - \int_A^B x^{k+1} f^{(k+1)}(x)x^{it} dx.$$

As $\frac{d}{dx} x^{it} = \frac{it}{x} x^{it}$, the previous relation follows by integration by parts:

$$\begin{aligned} it \int_A^B x^k f^{(k)}(x)x^{it} dx &= \int_A^B x^{k+1} f^{(k)}(x)(x^{it})' dx \\ &= \left[x^{k+1} f^{(k)}(x)x^{it} \right]_A^B - (k + 1) \int_A^B x^k f^{(k)}(x)x^{it} dx - \int_A^B x^{k+1} f^{(k+1)}(x)x^{it} dx. \end{aligned}$$

□

Corollary 4.5. *Let $f : [A, B] \rightarrow \mathbb{R}$ with $A, B \in [0, \infty]$ be a piecewise C^1 function. If f is non-negative, f' is non-positive, $f \in L^1(A, B)$, $f' \in L^1_1(A, B)$ and for all $t \in \mathbb{R}$: $[xf(x)x^{it}]_A^B = 0$, then:*

$$\langle t \rangle \left| \int_A^B f(x)x^{it} dx \right| \leq \int_A^B f(x) dx,$$

where $\langle t \rangle = (1 + t^2)^{1/2}$.

Proof. From Lemma 4.4 with $k = 1$ one obtains:

$$\forall t \in \mathbb{R} \quad (1 + it) \int_A^B f(x)x^{it} dx = - \int_A^B x f'(x)x^{it} dx.$$

As $A, B \geq 0$ and $f' \leq 0$, using this identity twice, for $t \neq 0$ and for $t = 0$, we get

$$\langle t \rangle \left| \int_A^B f(x)x^{it} dx \right| \leq \int_A^B |x f'(x)| dx = \int_A^B f(x) dx.$$

□

Lemma 4.6. *Let $n, K > 0, q \in \mathbb{R}$ and $f = \frac{\operatorname{erfc}^n}{\operatorname{erfc}^n + K}$. There exists $x_q > 0$ such that the function $g_q : x \in [x_q, \infty) \mapsto f(x)x^{q-1}$ is decreasing. Let $\tilde{q} = \inf E_q$ where $E_q = \{c \geq 0 \mid g'_q(x) < 0 \forall x \geq c\}$. The function $q \mapsto \tilde{q}$ is increasing and $\tilde{q} = (q/(2n))^{1/2} + o(q^{1/2})$ as $q \rightarrow \infty$.*

Proof. As $f > 0$, the inequality $g'_q(x) \leq 0$ is equivalent to:

$$\frac{f'(x)}{f(x)} \leq -\frac{q-1}{x}. \tag{4.5}$$

Let us compute $\frac{f'}{f}$. To do so, let $u = \operatorname{erfc}^n$, so that: $f = \frac{u}{u+K}$. We have:

$$\frac{f'}{f} = \frac{u'}{u} \frac{K}{u+K} = n \frac{\operatorname{erfc}'}{\operatorname{erfc}} \frac{K}{u+K}. \tag{4.6}$$

The derivative of erfc is given by: $\operatorname{erfc}'(x) = -2\pi^{-1/2}e^{-x^2}$. And, as x tends to $+\infty$: $\operatorname{erfc}(x) = \pi^{-1/2}x^{-1}e^{-x^2} + o(x^{-1}e^{-x^2})$. Thus, as x tends to $+\infty$:

$$\frac{f'(x)}{f(x)} = n \frac{\operatorname{erfc}'(x)}{\operatorname{erfc}(x)}(1 + o(1)) = -2nx + o(x). \tag{4.7}$$

This asymptotics proves that the inequality (4.5) is satisfied for large enough values of x . As a consequence for every q in \mathbb{R} the set E_q is not empty, which justifies the definition of \tilde{q} . Note that the definition of \tilde{q} implies: $g'_q(\tilde{q}) = 0$, that is: $\frac{f'(\tilde{q})}{f(\tilde{q})} = -\frac{q-1}{\tilde{q}}$, using (4.5).

Let $q_1 \geq q_2$ be two real numbers. In order to show that $\tilde{q}_2 \leq \tilde{q}_1$, it is enough to prove that $g'_{q_1}(\tilde{q}_2) \geq 0$. This holds because:

$$g'_{q_1}(\tilde{q}_2) = \tilde{q}_2^{q_1-2}(f'(\tilde{q}_2)\tilde{q}_2 + f(\tilde{q}_2)(q_1 - 1)) \geq \tilde{q}_2^{q_1-2}(f'(\tilde{q}_2)\tilde{q}_2 + f(\tilde{q}_2)(q_2 - 1)) = \tilde{q}_2^{q_1-q_2}g'_{q_2}(\tilde{q}_2) = 0.$$

To find the asymptotics on \tilde{q} , let us recall a lower bound on $\operatorname{erfc}(x)$ for $x \geq 0$:

$$\frac{1}{x + (x^2 + 2)^{1/2}} \leq \frac{1}{2}\pi^{1/2} \exp(x^2) \operatorname{erfc}(x).$$

As the function $u = \operatorname{erfc}^n$ takes its values in $(0, 1]$, we have: $\frac{nK}{1+K} \leq \frac{nK}{u+K} \leq n$. Consequently, thanks to (4.6):

$$-n \left(x + (x^2 + 2)^{1/2} \right) \leq \frac{f'(x)}{f(x)}. \tag{4.8}$$

Let $q > 1$ and set $x_q = \frac{q-1}{(2n)^{1/2}(n+q-1)^{1/2}}$. The inequality $-\frac{q-1}{x} \leq -n(x + (x^2 + 2)^{1/2})$ is equivalent to $x(x + (x^2 + 2)^{1/2}) \leq \frac{q-1}{n}$. A simple computation shows that this inequality is satisfied for $x = x_q$ (and becomes an equality). Thanks to (4.8), we conclude that x_q satisfies: $\frac{f'(x_q)}{f(x_q)} \geq -\frac{q-1}{x_q}$, which leads to $\tilde{q} \geq x_q$, by definition of \tilde{q} and by (4.5). This last inequality implies that \tilde{q} tends to $+\infty$ as q tends to $+\infty$. Finally we get the asymptotics for \tilde{q} , using (4.7):

$$-2n\tilde{q} + o(\tilde{q}) = \frac{f'(\tilde{q})}{f(\tilde{q})} = -\frac{q-1}{\tilde{q}}.$$

□

Now, we are in position to prove Proposition 4.3.

Proof of Proposition 4.3. The function J_1 is written:

$$J_1(x) = H_1(c_0 \operatorname{erfc}(x)) = f(x) \mathbb{1}_{x \geq \alpha} + K \mathbb{1}_{0 < x < \alpha},$$

with: $f(x) = \frac{\operatorname{erfc}(x)^n}{\operatorname{erfc}(x)^n + c_0^{-n} K_{1/2}^n}$ and $\alpha = \operatorname{erfc}^{-1}(a/c_0)$.

From the estimate for erfc at $+\infty$, given in the proof of Lemma 4.6, the function J_2 is in L_k^1 for every $k > -1$. Thus $\mathcal{M}J_1$ is holomorphic on the right half-plane, see Proposition 2.5. Using Lemma 3.2 on the vertical line $\frac{1-r}{2} + i\mathbb{R}$ with $\frac{1-r}{2} > 0$, as for the proof of Proposition 4.2, it amounts to bounding $|s\mathcal{M}J_1(s)|$, from above or from below, on the vertical lines $q + i\mathbb{R}$, for $q > 0$.

Then the Mellin transform of J_1 at $s = q + it$ is given by:

$$\mathcal{M}J_1(s) = K \int_0^\alpha x^{s-1} dx + c_0^n \int_\alpha^{+\infty} f(x)x^{s-1} dx = K \frac{\alpha^s}{s} + c_0^n \int_\alpha^{+\infty} f(x)x^{q-1}x^{it} dx.$$

For any $a \geq 0, q > 0$ and $s \in q + i\mathbb{R}$ we have:

$$|\mathcal{M}J_1(s)| \leq K \frac{\alpha^q}{q} + c_0^n \int_\alpha^{+\infty} f(x)x^{q-1} dx,$$

which is finite.

Let $q > 0$. According to Lemma 4.6 the function $x \mapsto f(x)x^{q-1}$ is decreasing for $x \geq x_0$. Let $a < c_0 \operatorname{erfc}(x_0)$ so that $\alpha = \operatorname{erfc}^{-1}(a/c_0) \geq x_0$. Let $g(x) = f(x)x^{q-1} \mathbb{1}_{x \geq \alpha}$. For every $t \in \mathbb{R} : [f(x)x^{it}]_{x_0}^\infty = 0$ because f vanishes for $x \leq \alpha$ and $x_0 \leq \alpha$, and $g(x) = \pi^{-n/2}x^{-n+q-1}e^{-nx^2} + o(x^{-n+q-1}e^{-nx^2})$. Then Corollary 4.5 can be applied to the function g , with $A = \alpha, B = +\infty$, for $s \in q + i\mathbb{R}$, to give:

$$\begin{aligned} |s\mathcal{M}J_1(s)| &\leq K |\alpha^s| + c_0^n \frac{|s|}{\langle t \rangle} \left| \int_\alpha^\infty f(x) x^{s-1} dx \right| \\ &\leq K \alpha^q + c_0^n \max(1, q) \int_\alpha^\infty f(x)x^{q-1} dx < \infty, \end{aligned}$$

because: $\frac{|s|}{\langle t \rangle} \in [q, 1] \cup [1, q]$, either $q \leq 1$ or $q \geq 1$.

For small values of a , the first term dominates the second one. The same calculation as above leads to:

$$|s\mathcal{M}J_1(s)| \geq K \alpha^q - c_0^n \max(1, q) \int_\alpha^\infty f(x)x^{q-1} dx,$$

This latter expression is equivalent to $K \alpha^q$ as α tends to $+\infty$, therefore, it is positive for large values of α . □

The smallness condition on a is needed for the observability inequality to be true. Indeed, for $a = c_0$ we have $H_1 = H_0$ so that $J_1 = J_0$ and no inequality of the last type holds. This assertion is a consequence of Theorem 4.7.

Third and finally, let us consider the case of the Hill function H_0 defined by (1.2). First, explicitly computing the derivatives of J_0 shows that the Mellin transform $\mathcal{M}J_0$ has a fast decay on vertical lines. Consequently on vertical lines of the right half-plane, and for any $k \in \mathbb{N}$, the function $|s^k \mathcal{M}J_0(s)|$ is bounded from above and

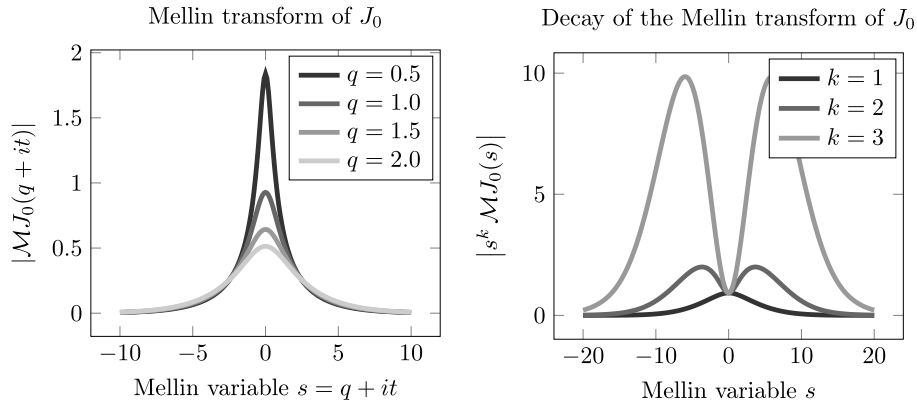


FIGURE 4. The Mellin transform $|\mathcal{M}J_0(s)|$, with $s = q + it$, for some values of q (left panel) and $|s^k \mathcal{M}J_0(s)|$, for some values of k (right panel), for $s \in 1 + i\mathbb{R}$. The functions are bounded from above but decay faster than any power function, see Theorem 4.7 and Lemmas 4.9, 4.10.

is not bounded from below. This is illustrated in Figure 4. As a consequence, no observability inequality of the previous type holds. Second, we prove an identifiability result for the operator I_0 based on these estimates.

Theorem 4.7. *Let $r < 1$.*

- *There exists $C > 0$ such that, for every ρ in L^2_r , we have:*

$$\|I_0[\rho]\|_{L^2_{\frac{r-3}{2}}} \leq C \|\rho\|_{L^2_r}.$$

- *Let $k \in \mathbb{N}$. There exists no constant $C \geq 0$ such that the observability inequality:*

$$\left\| (I_0[\rho])^{(k)} \right\|_{L^2_{2k + \frac{r-3}{2}}} \geq C \|\rho\|_{L^2_r},$$

holds for every function $\rho \in L^2_r$.

To prove Theorem 4.7 we show that the function $\mathcal{M}J_0$ decays faster than polynomially on vertical lines by proving that J_0 belongs to some Schwartz space.

Definition 4.8. Let $\mathcal{S}[0, \infty)$ be the space of functions f in $C^\infty([0, \infty), \mathbb{C})$ which satisfy:

$$\forall j \in \mathbb{N}, k \in \mathbb{N} \quad \lim_{x \rightarrow \infty} f^{(j)}(x) x^k = 0.$$

If f is a function of the Schwartz space $\mathcal{S}(\mathbb{R})$ then $f \mathbb{1}_{x \geq 0}$ is in $\mathcal{S}[0, \infty)$ (the converse is also true thanks to Borel’s lemma).

Lemma 4.9. *Let $f \in \mathcal{S}[0, \infty)$. Its Mellin transform $\mathcal{M}f$ is holomorphic on the right half-plane, and:*

$$\forall q > 0 \forall k \in \mathbb{N} \exists C \geq 0 \forall t \in \mathbb{R} : |\mathcal{M}f(q + it)| \leq C \langle t \rangle^{-k},$$

where $\langle t \rangle = (1 + t^2)^{1/2}$.

Proof of Lemma 4.9. Let $f \in \mathcal{S}[0, \infty), q > 0$. By the definition of $\mathcal{S}[0, \infty)$ for every l in \mathbb{N} and $k > -1$, the function $x \mapsto x^k f^{(l)}(x)$ is in L^1 . Proposition 2.5 implies that $\mathcal{M}f$ is holomorphic on the right half-plane.

Lemma 4.4 with $g(x) = f(x)x^{q-1}$ yields:

$$\mathcal{M}f(q + it) = \int_0^\infty f(x)x^{q-1}x^{it} dx = \sum_{j=0}^{k-1} (-1)^j Q_j(t) \left[x^{j+1} g^{(j)} x^{it} \right]_0^\infty + (-1)^k Q_{k-1}(t) \int_0^\infty x^k g^{(k)}(x) x^{it} dx,$$

where $Q_j(t) = \left(\prod_{l=0}^j (1 + l + it) \right)^{-1}$.

To prove this lemma it is enough to show that the terms between brackets vanish and that the last integral is finite.

Let $l, k \in \mathbb{N}$. By the Leibniz rule, we have:

$$x^l g^{(k)}(x) = \sum_{j=0}^k \binom{k}{j} f^{(k-j)}(x) (x^{q-1})^{(j)} x^l = \sum_{j=0}^k \binom{k}{j} (q-1)_j f^{(k-j)}(x) x^{q+l-1-j}.$$

For $l = k + 1$ and for $x = 0$ this expression vanishes because $f^{(k-j)}(0)$ is finite and: $q + k - j \geq q > 0$. As x tends to ∞ the expression tends to 0 as: $f^{(k-j)}(x) x^{q+k-j} \rightarrow 0$.

For $l = k$ this expression shows that the integral $\int_0^\infty x^k |g^{(k)}(x)| dx$ is finite because for every $j \in \{0, \dots, k\}$: $x \mapsto x^{q-1+j} f^{(j)}(x)$ is in L^1 because $q - 1 + j \geq q - 1 > -1$. Then:

$$|\mathcal{M}f(q + it)| \leq C |Q_{k-1}(t)| = C \langle t \rangle^{-k} + o(\langle t \rangle^{-k}).$$

□

Assuming that J_0 belongs to $\mathcal{S}[0, \infty)$, which is the main statement in Lemma 4.10, we are in a position to prove Theorem 4.7.

Lemma 4.10. *Let $n > 0$ and J_0 be the function defined by (1.2), (3.2). The function J_0 is in $\mathcal{S}[0, \infty)$.*

The proof of Lemma 4.10 is given in Appendix A.

Proof of Theorem 4.7. As in the proof of Lemma 3.2, thanks to (3.10), (3.11), the inequalities:

$$\left\| (\mathcal{I}_0[\rho])^{(k)} \right\|_{L^2_{2k + \frac{r-3}{2}}} \geq C \|\rho\|_{L^2_r} \tag{4.9}$$

and

$$\|(s)_k \mathcal{M}J_0(-2s) \mathcal{M}\rho(2s + 1)\|_{L^2(\frac{r-1}{4} + i\mathbb{R})} \geq C \|\mathcal{M}\rho(2s + 1)\|_{L^2(\frac{r-1}{4} + i\mathbb{R})} \tag{4.10}$$

are equivalent (up to some explicit constants depending on q, k). As in the proof of Lemma 3.2, the same equivalence is true changing all \geq signs to \leq signs.

Lemmas 4.9, 4.10 imply that $|\mathcal{M}J_0|$ is bounded from above on $\frac{1-r}{2} + i\mathbb{R}$ so that (4.10), with \leq instead of \geq , holds, which concludes the proof of the first statement.

We suppose that the second statement of the theorem is false so that there exists a constant $C > 0$ such that the inequality (4.10) holds for every $\rho \in L^2_r$. Let $s_0 \in \frac{r-1}{4} + i\mathbb{R}$ and $\delta > 0$. As the map $L^2_r \ni \rho \mapsto \mathcal{M}\rho(2s + 1) \in$

$L^2\left(\frac{r-1}{4} + i\mathbb{R}\right)$ is onto (in fact it is an isometry up to a multiplicative constant), we can find $\rho \in L^2_r$ such that $\mathcal{M}\rho(2s+1) = \mathbb{1}_{s_0+i[-\delta,\delta]}(s)$. For this choice of ρ , (4.10) is localized:

$$\frac{1}{2\delta} \int_{s_0-i\delta}^{s_0+i\delta} |\mathcal{M}J_0(-2s)|^2 |(s)_k|^2 ds \geq C.$$

Thanks to Lemmas 4.9, 4.10 the function J_0 belongs to L^2_q for every $q > -1$, thus, $\mathcal{M}J_0 \in L^2(\tilde{q} + i\mathbb{R})$ for $\tilde{q} > 0$ (cf. Thm. 2.11). In particular $|\mathcal{M}J_0(-2s)|^2 |(s)_k|^2$ is in L^1_{loc} , so, making $\delta \rightarrow 0$, the Lebesgue differentiation theorem shows that at almost every point s_0 :

$$|\mathcal{M}J_0(-2s_0)| |(s_0)_k| \geq C.$$

In other words $|\mathcal{M}J_0|$ has at most a polynomial decay on vertical lines $\frac{1-r}{2} + i\mathbb{R}$, which is a contradiction with Lemmas 4.9, 4.10. This concludes the proof. \square

Proposition 4.11. *Let $r < 0$ and $\rho \in L^1_r$. We consider the operator $I_0[\rho]$ defined by (1.1), (1.2), (1.3). If there exists a non empty open set U of $(0, \infty)$ such that:*

$$\forall t \in U \quad I_0[\rho](t) = 0,$$

then $\rho = 0$ a.e. on $(0, \infty)$.

Proof of Proposition 4.11. Lebesgue's dominated convergence theorem for analytic functions implies that $I_0[\rho]$ is an analytic function on $(0, \infty)$. For every $x \in [0, \infty)$, the function $\rho(x)H_0(c(\cdot, x))$ is analytic as erfc and power functions are analytic. For the domination part let $\eta > 0$. As for $t \geq \eta$: $\forall x \geq 0$ $\rho(x)H_0(c(t, x)) \leq \rho(x)H_0(c(\eta, x))$, it remains to show that $\rho H_0(c(\eta, \cdot))$ is an L^1 function. At $+\infty$, we have: $H_0(c(\eta, x)) = \pi^{-n/2} 2^n D^{n/2} \eta^{n/2} x^{-n} \exp(-\frac{nx^2}{4D\eta}) + o\left(x^{-n} \exp(-\frac{nx^2}{4D\eta})\right)$, so that $\int_1^\infty \rho(x)H_0(c(\eta, x)) dx$ is finite because $\rho \in L^1_r$. At 0 we have: $H_0(c(\eta, 0)) = (1 + c_0^{-n} K_{1/2}^n)^{-1} > 0$, and, as $r \leq 1$: $\int_0^1 \rho(x) dx \leq \int_0^1 \rho(x)x^{r-1} dx$ is finite so that $\int_0^1 \rho(x)H_0(c(\eta, x)) dx$ is also finite.

As $I_0[\rho]$ vanishes on U , the principle of permanence implies that it vanishes on the connected set $(0, \infty)$:

$$\forall t \in (0, \infty) \quad I_0[\rho](t) = 0.$$

Taking the Mellin transform of this relation, using Definition (3.2), we obtain:

$$\forall s \in r + i\mathbb{R} \quad 2^{-s} D^{-s/2} \mathcal{M}J_0(-s) \mathcal{M}\rho(s+1) = 0.$$

Thanks to Lemmas 4.10, 4.9, the function $\mathcal{M}J_0$ is holomorphic on the right half-plane, which contains the line $-r + i\mathbb{R}$, because $r < 0$. The function $\mathcal{M}J_0$ is not identically zero so $\mathcal{M}J_0$ can vanish only on a set $-Z$ having no accumulation point. The previous relation implies that $\mathcal{M}\rho = 0$ on $r+1 + i\mathbb{R} \setminus (1+Z)$. As $\rho \in L^1_r$ the function $\mathcal{M}\rho$ is continuous on the vertical line $r+1 + i\mathbb{R}$, so that $\mathcal{M}\rho$ is identically zero on $r+1 + i\mathbb{R}$. The Inversion Theorem 2.7 provides the result. \square

5. NUMERICAL ILLUSTRATION

In this section we present some numerical simulations based in modeled current representing experimental data. The parameters in equations (1.1), (1.2), (1.3) have been experimentally estimated to be $n = 1.7$, $K_{1/2} = 0.17$ [μM] (see [2, 10] and the references therein). The value of the diffusion coefficient $D > 0$ does not play any important role in our analysis, so that it has been arbitrarily set to $D = 1$ [$\text{m}^2 \text{s}^{-1}$]. On the other hand,

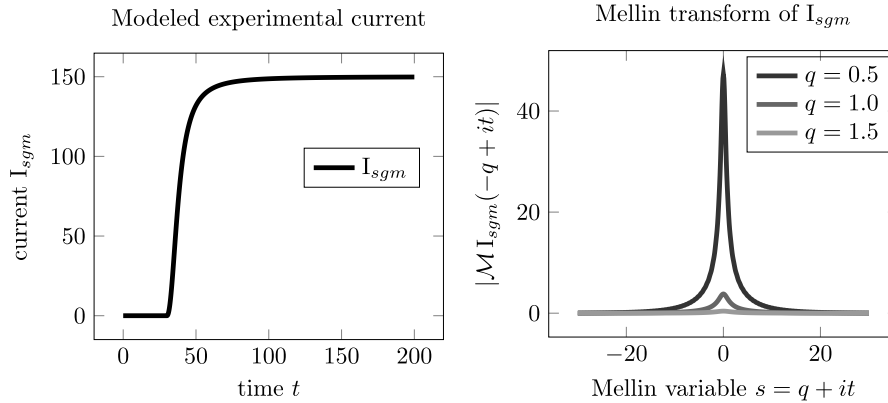


FIGURE 5. Model function of the total current I_{sgm} (left panel), defined by (5.1), and its Mellin transform $t \mapsto |\mathcal{M}I_{sgm}(-q + it)|$ for some values of q (right panel).

the reference value for the initial concentration c_0 has been fixed to $c_0 = 1$ [μM], to show clearly the important behaviors in the figures.

As already mentioned in the Introduction, the experimental procedures developed by S.J. Kleene allow the current generated by depolarization to be measured. The profiles founded in some laboratory applications (see [4, 8] or [17]) are very similar to a delayed sigmoidal function (Fig. 5 (left)). Thus, in order to contrast numerical experiences with experimental data, in what follows, the total measured current is modeled by the function

$$I_{sgm}(t) = \begin{cases} 0 & \text{if } t \leq t_D \\ I_{max} \left[1 + \left(\frac{K_I}{t-t_D} \right)^{n_I} \right]^{-1} & \text{if } t > t_D \end{cases} \quad (5.1)$$

In view of this way of modeling the total measured current, the results obtained in Propositions 4.2, 4.3 can be rephrased as follows: if the measured current I_{sgm} is in some well-defined weighted L^2 space, then the distribution ρ of the CNG channels is uniquely defined (in another, well-determined, weighted L^2 space) by (3.7).

In the sequel we consider the following model for the experimentally observed current (see [10] and the references therein):

The values used as parameters in the different numerical experiences are: $I_{max} = 150$ [pA], $n_I = 2.2$, $K_I = 100$ [ms], $t_D = 30$ [ms]. The function I_{sgm} is shown in Figure 5 (left).

Note that the derivative of I_{sgm} is in L^2_q , for some $q < 0$ so Proposition 4.3 (or Prop. 4.2) can be applied directly. If the data were noisy, a standard regularization method for an inverse problem with a finite degree of ill-posedness (see [6] for instance) could be applied to the data before applying Proposition 4.3. In this extend our numerical method consisting of Proposition 4.3 can be applied to any noisy experimental data. For the approximated operator $I_1[\rho]$ the distribution ρ can be found from the current I_{sgm} , as shown in Figure 6 if a has a small enough value.

For the operator $I_0[\rho]$ the distribution ρ cannot be found from the current I_{sgm} , even after a regularization, as shown in Figure 7. This is consistent with Theorem 4.7, which states that no observability inequality can be found for I_0 in some weighted L^2_q spaces.

Technical aspects. As seen in the previous sections, the functions $\mathcal{M}J_0, \mathcal{M}J_1, \mathcal{M}J_2$ are holomorphic on the right half-plane. As $t_D > 0, n_I > 0, I_{sgm}$ is in L^1_k for every $k < -1$, then, $\mathcal{M}I_{sgm}$ is holomorphic on the left half-plane. Therefore the quotient $\frac{\mathcal{M}I_{sgm}(s/2)}{\mathcal{M}J_1(-s)}$ is meromorphic on the left half-plane. The inverse Mellin transform of this function has been computed on different vertical lines, whose abscissas are $q < 0$.

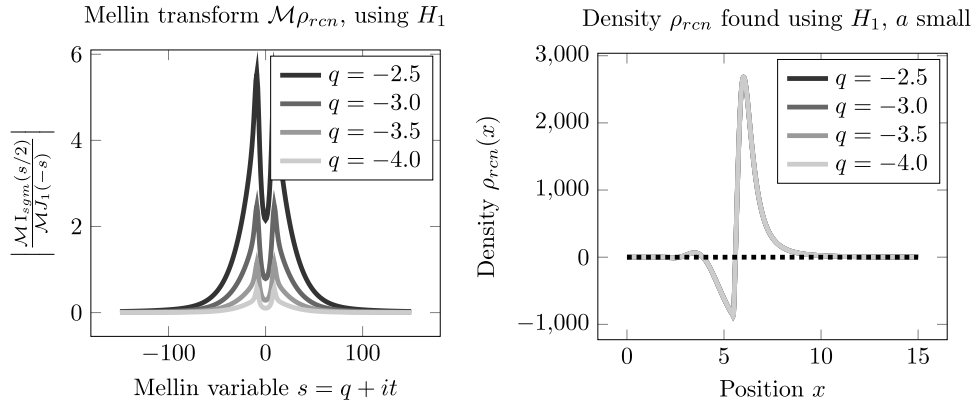


FIGURE 6. (left panel) Function in Mellin variables to be inverted to reconstruct the density ρ_{rcn} using the approximated Hill function H_1 given by (1.4). (right panel) The corresponding reconstructed CNG channels distribution ρ_{rcn} , for the largest value of a , $a = 0.1573$, for which Proposition 4.3 holds. The computed density $\rho_{rcn} = \mathcal{M}_q^{-1} \left(\frac{\mathcal{M}I_{sgm}(s/2)}{\mathcal{M}J_1(-s)} \right) \in L^2_q$ does not depend on the weight $q \in [-4, -2]$: the curves are superimposed.

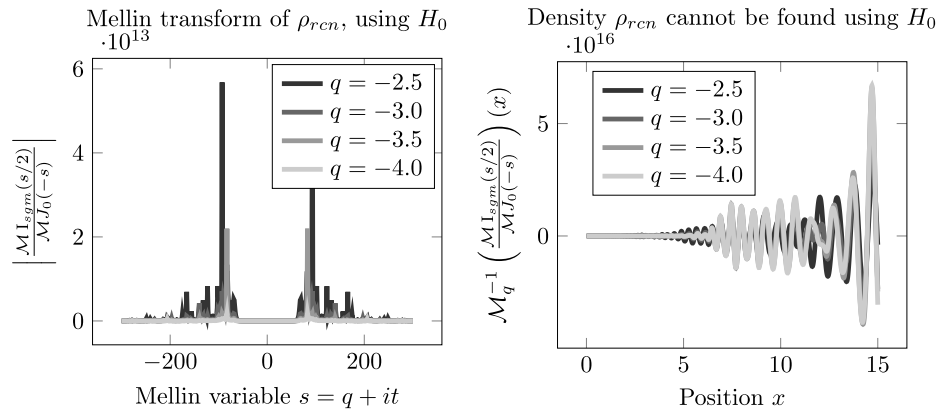


FIGURE 7. (left panel) Function in Mellin variables to be inverted to reconstruct the density ρ_{rcn} using the exact Hill function. (right panel) The corresponding CNG channels distribution ρ_{rcn} cannot be reconstructed, see Theorem 4.7.

As the quotient $\frac{\mathcal{M}I_{sgm}(s/2)}{\mathcal{M}J_1(-s)}$ does not vanish in the left half-plane, the distribution ρ does not depend on $q < 0$. More details regarding this kind of results can be found in [3] for instance. Figure 6 illustrates Proposition 4.3. For the numerical simulations, the parameter a is taken to be the biggest for which the quotient defined above does not vanish in the strip $\{x + it \mid x \in [-4, -2], t \in \mathbb{R}\}$, that is $a = 0.1573$.

In previous works [9, 10, 11], as ρ stands for a density, a penalization method is introduced to ensure $\rho > 0$. Note that, if the negative part of ρ_{rcn} is removed then its profile is similar to the one exhibited in these works.

6. CONCLUSIONS

We focussed on the problem of finding the spatial distribution of CNG ion channels from the experimental current data, following [2, 5, 9, 10, 11]. The self-similar structure of the integral inverse problem (1.1), (1.2), (1.3) allowed us to use the Mellin transform, and to obtain a thorough comprehension of it. It permitted us to

reduce its study to estimating some Mellin transform, on vertical lines of the complex plane. To do so, explicit computations were carried out using techniques inspired by the stationary phase method.

As a result the inverse problem studied has been shown not to be controllable in some weighted L^2 spaces. The kernel of the integral operator is smooth and the associated inverse problem has an infinite degree of ill-posedness. This conclusion could probably be linked to the fact that for the original problem, introduced in [11], certain numerical computations indicate that it is ill-conditioned. We also introduced a better approximation than the one already studied, for which we performed numerical simulations and provided estimates. In this case the kernel of the integral operator is at most continuous and the associated inverse problem has a finite degree of ill-posedness (which is 1). The profiles obtained from the experimental current data consolidate the ones obtained in [9, 10, 11].

For a kernel obtained by linear interpolation from cAMP concentration *versus* current data functions instead of H_0 , see [13], which is thus continuous but not smooth, our method could be applied but no new kind of mathematical result is expected.

To go further, one could study the inverse problem (1.1), (1.2) where c is defined as the solution of the linear heat equation:

$$\begin{cases} \partial_t c - D \partial_{xx} c &= 0, & t > 0, x \in (0, L), \\ c(t, 0) &= c_0, & t > 0, \\ \partial_x c(t, L) &= 0, & t > 0, \\ c(0, x) &= 0, & x \in (0, L). \end{cases}$$

If the Hill function (1.2) is changed into its Taylor polynomial extension around c_0 , and if this polynomial has a degree $m \leq 8$, then [5] proves that the resulting integral operator I is identifiable in L^2 . To go further, a first step, could, be to study this problem without approximating the Hill function. Studying the complete inverse problem for the original model could be a further step. It would seem that these two problems cannot be solved using the Mellin transform technique alone, as no self-similar structure is directly involved.

APPENDIX A. PROOF OF LEMMA 4.10

We recall the Faà di Bruno formula, first proved by L.F.A. Arbogast see [1]:

$$(f \circ g)^{(k)} = \sum_{\substack{(m_1, \dots, m_k) \in \mathbb{N}^k \\ \sum_{j=1}^k j m_j = k}} \frac{k!}{\prod_{j=1}^k m_j! j!^{m_j}} f^{(\sum_{j=1}^k m_j)} \circ g \prod_{j=1}^k (g^{(j)})^{m_j}.$$

This formula allows us to make explicit computations, to prove that the functions appearing in Lemmas 4.10 are in $\mathcal{S}(0, \infty)$.

Lemma A.1. *The function erfc is of the class C^∞ on $[0, \infty)$. For every $k \in \mathbb{N}^*$:*

$$\operatorname{erfc}^{(k)}(x) = P_k(x) \exp(-x^2),$$

where P_k is a polynomial which has a degree of $k - 1$ whose leading coefficient is $\pi^{-1/2}(-2)^k$. In particular, as x tends to ∞ :

$$\operatorname{erfc}^{(k)}(x) = \pi^{-1/2}(-2)^k x^{k-1} e^{-x^2} + o(x^{k-1} e^{-x^2}).$$

Proof. The proof is by induction on $k \in \mathbb{N}^*$. By the definition of erfc : $\operatorname{erfc}'(x) = -2\pi^{-1/2} \exp(-x^2)$ and with simple calculations we have:

$$P_{k+1} = -2XP_k + P'_k.$$

□

Lemma A.2. *The function H defined by (1.2) is of the class C^∞ on $[0, \infty)$. For $n \geq 0$ it satisfies for every $k \in \mathbb{N}^*$:*

$$H_0^{(k)}(x) = \frac{P_k(x)}{(x^n + K_{1/2}^n)^{k+1}},$$

where $P_k(x) = (-1)^{k-1}(n-k-1)_k K_{1/2}^n x^{(n-1)k} + \dots + (n)_k K_{1/2}^{nk} x^{n-k}$.

In particular:

$$H_0^{(k)}(x) = K_{1/2}^{nk} (n)_k x^{n-k} + o(x^{n-k}).$$

Proof. The proof is by induction on $k \in \mathbb{N}^*$. Simple calculations lead to: $P_1(x) = nK_{1/2}^n x^{n-1}$ and:

$$P_{k+1}(x) = x^n P'_k(x) - (k+1)nx^{n-1}P_k(x) + K_{1/2}^n P'_k(x).$$

It follows that the leading term in $P_k(x)$ as x tends to $+\infty$ is of the form $a_k x^{(n-1)k}$ where a_k satisfies:

$$a_1 = nK_{1/2}^n, \quad a_{k+1} = a_k((n-1)k - n(k+1)) = -a_k(n+k).$$

As $n \geq 0$, the leading term in $P_k(x)$ as x tends to 0 is of the form $b_k x^{n-k}$ where b_k satisfies:

$$b_1 = nK_{1/2}^n, \quad b_{k+1} = b_k(n-k)K_{1/2}^n.$$

□

Lemma A.3. *For $n > 0$, the function J_0 defined by (1.2), (1.3), (3.2) is in $\mathcal{S}[0, \infty)$.*

Proof. The function is of the class $C^\infty(0, +\infty)$ because erfc is of this class and $n > 0$. For every integer $k \in \mathbb{N}$, $H^{(k)}(c_0)$ and $\operatorname{erfc}^{(k)}(0)$ are finite, thus for every $k \in \mathbb{N}$, $J_0^{(k)}(0)$ is finite.

Applying the Faà di Bruno formula one gets, for $x \geq 0$:

$$J_0^{(k)}(x) = \sum_{\substack{(m_1, \dots, m_k) \in \mathbb{N}^k \\ \sum_{j=1}^k j m_j = k}} \frac{k!}{\prod_{j=1}^k m_j! j!^{m_j}} H^{(\sum_{j=1}^k m_j)}(c_0 \operatorname{erfc}(x)) \prod_{j=1}^k (c_0 \operatorname{erfc}^{(j)}(x))^{m_j}.$$

As x tends to $+\infty$, from the previous lemmas, we have, for $S = \sum_{j=1}^k m_j$:

$$H^{(S)}(c_0 \operatorname{erfc}(x)) = K_{1/2}^{-n}(n)_S (c_0 \operatorname{erfc}(x))^{n-S} (1 + o(1)) = K_{1/2}^{-n}(n)_S (c_0 \pi^{-1/2} x^{-1} \exp(-x^2))^{n-S} (1 + o(1)).$$

Then, for $\sum_{j=1}^k j m_j = k$ and $\sum_{j=1}^k m_j = S$:

$$\begin{aligned} & H^{(\sum_{j=1}^k m_j)}(c_0 \operatorname{erfc}(x)) \prod_{j=1}^k \left(c_0 \operatorname{erfc}^{(j)}(x) \right)^{m_j} \\ &= K_{1/2}^{nS}(n)_S (c_0 \pi^{-1/2} x^{-1} \exp(-x^2))^{n-S} \prod_{j=1}^k c_0^{m_j} (\pi^{-1/2} (-2)^j x^{j-1} \exp(-x^2))^{m_j} (1 + o(1)) \\ &= (-2)^k K_{1/2}^{nS}(n)_S c_0^n \pi^{-n/2} x^{k-n} \exp(-nx^2) \end{aligned}$$

Let us denote:

$$C(n, k) = (-2)^k k! c_0^n \pi^{-n/2} \sum_{\substack{(m_1, \dots, m_k) \in \mathbb{N}^k \\ \sum_{j=1}^k j m_j = k}} (n)_{\sum_{j=1}^k m_j} K_{1/2}^{n \sum_{j=1}^k m_j} \left(\prod_{j=1}^k m_j! j^{m_j} \right)^{-1}.$$

If $C(n, k) \neq 0$, the previous calculations lead to:

$$J_0^{(k)}(x) = C(n, k) x^{k-n} \exp(-nx^2) (1 + o(1)).$$

If $C(n, k) = 0$: $J_0^{(k)}(x) = o(x^{k-n} \exp(-nx^2))$. In both cases, for every $j \in \mathbb{N}$: $(J_1)^{(k)} = o(x^j)$, which concludes the proof. □

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