Title: The Mathematical Legacy of Andrzej Lasota

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THE MATHEMATICAL LEGACY
OF ANDRZEJ LASOTA*

Introduction

Professor Andrzej Lasota (1932–2006) was a Polish mathematician with wide ranging interests in dynamical systems, probability theory and ergodic theory who saw the inter-relationships between all three and who successfully synthesized these apparently disparate fields. He used that synthesis to both further mathematical research as well as to investigate problems in biology. One of his over-riding interests was the way in which seemingly "random" or "probabilistic" processes (in a mathematical sense) could actually be thought of as equivalently coming from deterministic dynamics.

How did we each come to know him and his work? Michael C. Mackey met Lasota in Cracow in 1977 through his collaborator Dr. Maria Ważewska-Czyżewska, a hematologist and daughter of Professor Tadeusz Ważewski. That meeting blossomed into an almost 30-year-long friendship and collaboration in biomathematics. Marta Tyran-Kamińska met Lasota during her mathematical studies at the University of Silesia in Katowice in 1992 and did her Ph.D. under his supervision. Hans-Otto Walther met Lasota during a year at Michigan State University, 1979–1980, where Pavel Brunovský was also visiting, and they had all been brought together by Shui-Nee Chow.

Dynamical Systems and Evolution of Densities

L et $(X, \mathcal{A})$ be a measurable space and $S \colon X \to X$ be a measurable transformation. A normalized (probability) measure $\mu \colon \mathcal{A} \to [0,1]$ is said to be *invariant* under S if

$$\mu(S^{-1}(A)) = \mu(A) \quad \text{for all } A \in \mathcal{A}$$

and S is called a measure-preserving transformation on $(X, \mathcal{A}, \mu)$. The transformation S with invariant measure μ is called *ergodic* if any invariant set $A = S^{-1}(A)$, $A \in \mathcal{A}$, satisfies $\mu(A) = 0$ or $\mu(A) = 1$. Next in the hierarchy is the stronger property of mixing: S is called *mixing* if

$$\lim_{n \to \infty} \mu(A \cap S^{-n}(B)) = \mu(A)\mu(B) \quad \text{for all } A, B \in \mathcal{A}.$$

For a (non-invertible) transformation S, the strongest property is exactness: S is called *exact* if $S(A) \in \mathcal{A}$ for all $A \in \mathcal{A}$ and

$$\lim_{n \to \infty} \mu(S^n(A)) = 1 \quad \text{for all } A \in \mathcal{A}, \ \mu(A) > 0.$$

We now recall the concept of a transfer operator. Let $(X, \mathcal{A}, \mu)$ be a σ-finite measure space and let D be the subset of $L^1 = L^1(X, \mathcal{A}, \mu)$ containing all densities

$$D = \{f \in L^1 : f \geq 0, \ \|f\| = 1\}.$$

If S is nonsingular on $(X, \mathcal{A}, \mu)$, i.e. $\mu(S^{-1}(A)) = 0$ whenever $\mu(A) = 0$ for any $A \in \mathcal{A}$, then the operator $P \colon L^1 \to L^1$ defined by

$$\int_A Pf(x)\,\mu(dx) = \int_{S^{-1}(A)} f(x)\,\mu(dx) \quad \text{for } A \in \mathcal{A}, f \in L^1, \qquad (1)$$

is called the *Frobenius–Perron operator* (or *transfer operator*) associated with S. The operator P has an *invariant density* $f_* \in D$, i.e. $Pf_* = f_*$, if and only if the probability measure μ_{f_*}

$$\mu_{f_*}(A) = \int_A f_*(x)\,\mu(dx), \quad A \in \mathcal{A},$$

is invariant under S.

If S is nonsingular on $(X, \mathcal{A}, \mu)$ and the Frobenius–Perron operator P has an invariant density f_* then we write (S, f_*) to indicate that the measure μ_{f_*} is invariant under S. If μ itself is a probability measure invariant under S then S is nonsingular on $(X, \mathcal{A}, \mu)$ and the constant function equal to 1 is an invariant density for P. Using the Frobenius–Perron operator we may reformulate the concepts of ergodicity, mixing, and exactness to classify density evolution.

Theorem 1. [23, Theorem 4.4.1] *Let P be the Frobenius–Perron operator associated with S and let f_* be an invariant density for P.*

1. *(S, f_*) is ergodic if and only if the sequence $\{\frac{1}{n}\sum_{k=0}^{n-1} P^k f\}$ is weakly convergent to f_* for all $f \in D$.*

2. *(S, f_*) is mixing if and only if the sequence $\{P^n f\}$ is weakly convergent to f_* for all $f \in D$.*

3. *(S, f_*) is exact if and only if the sequence $\{P^n f\}$ is strongly convergent to f_* for all $f \in D$.*

In 1973, Lasota and Yorke [26] proved the existence of an absolutely continuous invariant probability measure for piecewise expanding, C^2-transformations on a bounded interval. Their method turned out to be quite general and can be described as follows. Suppose $(V, \|\cdot\|_V)$ is a Banach space with norm $\|\cdot\|_V \geq \|\cdot\|$ such that V is densely embedded in L^1, the unit ball $\{f \in V : \|f\|_V \leq 1\}$ is compact in $(L^1, \|\cdot\|)$, and a Frobenius–Perron operator $P: L^1 \to L^1$ is such that $P: V \to V$ is bounded and for some constants $r \in (0, 1)$, $M \geq 0$, $k \in \mathbb{N}$, the following holds

$$\|P^k f\|_V \leq r\|f\|_V + M\|f\| \quad \text{for all } f \in V. \tag{2}$$

Then the operator P has an invariant density in V. For the one dimensional maps considered in [26] the space V was the space of functions with bounded variation. Condition (2) is usually referred to as the *Lasota–Yorke type inequality* in the theory of dynamical systems and it has been used in different settings [11, 2]. It gives a spectral decomposition of the operator P on the space V, where it acts as a quasi-compact operator, and it is related to the concept of asymptotic periodicity [10, 21, 13, 12]. In particular, mixing and exactness are equivalent properties when condition (2) holds.

In 1982, Lasota and Yorke [28] introduced the method of a lower bound function and proved the existence of an absolutely continuous invariant measure together with exactness of piecewise convex transformations on an interval. A linear operator $P: L^1 \to L^1$ that satisfies $Pf \geq 0$ and $\|Pf\| = \|f\|$ for all $f \geq 0$, $f \in L^1$ is called a *Markov* (or a *stochastic*) operator. If we restrict ourselves to only considering densities $f \in D$ then any linear operator P which when acting on a density again yields a density is a Markov operator. Thus the Frobenius–Perron operator is a Markov operator. Given a Markov operator the family $\{P^n\}$ is said to be *asymptotically stable* if there is $f_* \in D$ such that $Pf_* = f_*$ and

$$\lim_{n \to \infty} \|P^n f - f_*\| = 0 \quad \text{for all } f \in D.$$

An L^1 function h is a *nontrivial lower bound function* for $\{P^n\}$ if $h \geq 0$, $\|h\| > 0$ and

$$\lim_{n \to \infty} \|(P^n f - h)^-\| = 0 \quad \text{for all } f \in D.$$

This condition could be written in the alternate form

$$P^n f \geq h - \epsilon_n$$

where $\|\epsilon_n\| \to 0$ as $n \to \infty$, illustrating that a lower bound function is such that successive iterates of a density f by a Markov operator P are eventually above it. With these concepts, we can now state the result of [28] that has proved to be of considerable utility in a variety of settings.

Theorem 2. *$\{P^n\}$ is asymptotically stable if and only if $\{P^n\}$ has a nontrivial lower bound function.*

This method allowed simple proofs of exactness of piecewise expanding mappings on intervals or on the real line, as well as the results of [14] for expanding mappings on manifolds. Another context where Theorem 2 has found application is in dynamical systems with stochastic perturbations. Specifically, consider the following recurrence equation

$$x_{n+1} = S(x_n) + \xi_n,$$

where S is a transformation acting on $X = \mathbb{R}^d$ and $\{\xi_n\}$ is a sequence of independent random variables with density g. If f_n is the density of x_n then $f_{n+1} = P f_n$ and the Markov operator P is given by

$$Pf(x) = \int_X f(y) g(x - S(y)) \, dy,$$

which is a particular example of integral operators of the form

$$Pf(x) = \int_X k(x, y) f(y) \, \mu(dy),$$

where $k \colon X \times X \to [0, \infty)$ is a measurable function satisfying

$$\int_X k(x, y) \, \mu(dx) = 1$$

for almost all $y \in X$. An interesting class of integral Markov operators appeared in a simple model of the cell cycle [22] and its generalizations [8, 34, 24].

The lower bound function technique has also been applied in a continuous time setting [23, Section 11], where a family $\{P^t\}_{t \geq 0}$ of operators

on L^1 will be called a *stochastic semigroup* if each operator P^t is Markov and $\{P^t\}_{t \geq 0}$ is a strongly continuous semigroup on L^1. Asymptotic stability in continuous time arises in the study of long-term behavior of solutions of integro-differential equations

$$\partial_t u = Au - \lambda u + \lambda P u,$$

where P is an integral operator, $\lambda \geq 0$ is a constant, and A is the infinitesimal generator of a stochastic semigroup, in particular a first or second order differential operator, which we now recall. Given a set of ordinary differential equations

$$\frac{dx_i}{dt} = b_i(x), \qquad i = 1, \ldots, d \tag{3}$$

operating in a region of $\mathbb{R}^d$, whose solutions are defined for all times through a flow $\{S^t\}_{t \in \mathbb{R}}$, leads to the family of Frobenius–Perron operators

$$P^t f(x) = f(S^{-t}(x)) J^{-t}(x),$$

where J^{-t} is the Jacobian of the transformation S^{-t}. This gives the evolution equation for $f(t, x) = P^t f(x)$:

$$\frac{\partial f}{\partial t} = -\sum_{i=1}^{d} \frac{\partial(b_i f)}{\partial x_i}, \tag{4}$$

which will be recognized as the generalized Liouville equation. As an extension of the situation for ordinary differential equations, for stochastic differential equations of the form

$$dx = b(x)dt + \sigma(x)dW(t),$$

where x is a d-dimensional vector and $W(t)$ is a standard Wiener process, then the density $f(t, x) = P^t f(x)$ satisfies the Fokker–Planck equation

$$\frac{\partial f}{\partial t} = -\sum_{i=1}^{d} \frac{\partial(b_i f)}{\partial x_i} + \frac{1}{2} \sum_{i,j=1}^{d} \frac{\partial^2(a_{ij} f)}{\partial x_i \partial x_j}, \tag{5}$$

where $a_{ij}(x) = \sum_{k=1}^{d} \sigma_{ik}(x)\sigma_{jk}(x)$. For a review of asymptotic behavior of stochastic semigroups we refer to [33].

We end this section with a few remarks concerning continuous time systems. Let $\{S^t\}_{t \geq 0}$ be a semigroup of measurable transformations on $(X, \mathcal{A})$. A probability measure μ is invariant under $\{S^t\}_{t \geq 0}$ if μ is an

invariant measure under all S^t and it is called ergodic if sets invariant under all S^t are of measure zero or one. The concepts of mixing and exactness extend accordingly. Exactness will not occur for flows defined by (3), since each S^t is invertible. However, it might occur in infinite-dimensional phase-space, as will be indicated in the next section.

First-Order Partial Differential Equations

Motivated, no doubt, by [35] and inspired by the initial results in [27, 19], Lasota [20] considered the following

$$\frac{\partial u}{\partial t} + c(x)\frac{\partial u}{\partial x} = f(x, u) \tag{6}$$

with the initial condition

$$u(0, x) = v(x) \quad \text{for } x \in [0, 1]. \tag{7}$$

The functions $c \colon [0, 1] \to \mathbb{R}$ and $f \colon [0, 1] \times [0, \infty) \to \mathbb{R}$ satisfy

$$
\begin{aligned}
&c(0) = 0, \quad c(x) > 0 \quad \text{for } x \in (0, 1], \\
&f(x, u) \leq k_1 u + k_2 \quad \text{for } x \in [0, 1], u \geq 0, \\
&f(x, 0) = 0 \quad \text{for } x \in [0, 1].
\end{aligned}
$$

It was shown in [20] that under some regularity assumptions on c and f the solutions of equation (6) with the initial condition (7) define a semigroup $\{S^t\}_{t\geq 0}$ on the space $C_+([0, 1])$ of nonnegative continuous functions on $[0, 1]$ and the semigroup $\{S^t\}_{t\geq 0}$ has an interesting long-term behavior. Namely, $S^t v$ converges, as $t \to \infty$, to the same limit for each v with $v(0) > 0$ and $\{S^t\}_{t\geq 0}$ is chaotic in the sense of Auslander–Yorke [1] on a set $V \subseteq \{v \in C_+([0, 1]) \colon v(0) = 0\}$, which means that there is $v \in V$ such that the orbit $\{S^t v \colon t \geq 0\}$ is dense in V and that for each $v \in V$ the orbit $\{S^t v \colon t \geq 0\}$ is unstable. This extremely irregular behavior was later identified with exactness of $\{S_t\}_{t\geq 0}$ in [3, 4, 31, 32].

These results were used by Lasota and colleagues in [25] to understand the success that Maria Ważewska had had in treating patients who had developed aplastic anaemia due to chemotherapy, radiotherapy, or exposure to certain organic compounds. They developed a reasonably interesting and straightforward physiologically realistic model for the process. In terms of dimensionless variables the model was formulated as a reaction-convection equation for the normalized red cell precursor density $u(t, x)$ at time t and maturation level x:

$$\frac{\partial u}{\partial t} + c(x)\frac{\partial u}{\partial x} = \left[p(t, x, u) - \frac{\partial c}{\partial x}\right]u(t, x),$$

where

$$c(x) = \begin{cases} x, & 0 \le x \le 1, \\ 1, & 1 \le x, \end{cases}$$

is the normalized cell maturation velocity and

$$p(t, x, u) = \begin{cases} \lambda(1 - u(t, x)), & 0 \le x < 1, \\ 0, & 1 \le x < L + 1, \\ -\infty, & L + 1 \le x, \end{cases}$$

is the normalized relative proliferation rate. L is related to the range of maturation levels. Using this model they were able to precisely explain the successful treatment through a decrease in the cellular maturation rate which led to a minimization of the low levels of red blood cells during recovery periods.

Differential Delay Equations

Ważewska-Czyżewska and Lasota [35], in an examination of the dynamics of erythrocyte production, started from a time-age model for red blood cell development and derived the differential delay equation

$$\frac{dx}{dt} = -\gamma x + \beta e^{-\alpha x_\tau} \qquad x_\tau \equiv x(t - \tau), \tag{8}$$

and then studied aspects of the solution behavior both analytically and numerically. There is a unique steady state which is positive. Depending on the parameters it is either hyperbolic and stable (and thereby attracting), or it is a center, or it is hyperbolic and unstable. Numerical results suggest that in the first case the steady state is globally attracting. In [5] it is shown that in the last case there exists a periodic orbit which seems to be hyperbolic and stable, with a large domain of attraction. Periodic orbits as in [5] also arise in a supercritical local Hopf bifurcation. There are further Hopf bifurcations which result in other periodic orbits, all of them unstable.

Coincidentally Mackey and Glass [30], in an examination of the regulation of respiration, derived very similar equation

$$\frac{dx}{dt} = -\gamma x + \beta \frac{1}{1 + x_\tau^n} \qquad x_\tau \equiv x(t - \tau) \tag{9}$$

that had the same qualitative monotone decreasing nonlinearity as equation (8) and the same qualitative solution behavior.

In the same paper Mackey and Glass [30] also proposed a second model for the regulation of white blood cell production that was framed in terms of a differential delay equation given by

$$\frac{dx}{dt} = -\gamma x + \beta \frac{x_\tau}{1 + x_\tau^n} \qquad x_\tau \equiv x(t - \tau). \tag{10}$$

In studying equation (10), now known as the Mackey–Glass equation, the solution behavior of equation (10) is much richer than that of (8) or (9), since one can either have a globally stable steady state, or a Hopf bifurcation to a simple limit cycle which can then show further bifurcations to more complicated limit cycles satisfying the Sharkovsky sequence and displaying Feigenbaum scaling. Ultimately 'chaotic' solutions can ensue. We now know that this variety of solution behaviors and existence of multiple bifurcations is due to the non-monotone nature of the nonlinearity in (10). In what has to be one of the delicious ironies of life and research, the same year Lasota published a paper [18] in which he had considered an equation qualitatively identical to (10), but without knowing of the work published in [30]. The Lasota version was of the form

$$\frac{dx}{dt} = -\gamma x + \beta x_\tau^n e^{-x_\tau}, \tag{11}$$

so the nonlinearity had the same non-monotone character as in equation (10). Thus, from a historical perspective, differential delay equations of the form

$$\frac{dx}{dt} = -\gamma x + F(x_\tau), \tag{12}$$

with $F(y) \geq 0$, $F(0) = 0$, $F'(0) \geq 0$, $F'(y) = 0$ for some $y \in (0, \infty)$, $\lim_{y \to \infty} F(y) = 0$, should be known as Lasota–Mackey–Glass equations for their spectrum of solution behaviors.

Incidentally, let us mention that for (12) with certain special functions F it can be proved that chaotic solutions do exist, in case $\gamma > 0$ (see [9]) and in case $\gamma = 0$ (see [16, 17, 15]). However, these results do not cover (10) and (11), for which existence of chaotic motion remains an open problem.

The problem is related to a conjecture, formulated by Lasota in [18, Section 5], about existence of an invariant ergodic measure corresponding to equation (11), which we now recall with an obvious change of his notation. Let $C = C([-\tau, 0])$ be the space of continuous functions $\varphi \colon [-\tau, 0] \to \mathbb{R}$ with the supremum norm topology. Consider the mapping $S \colon C \to C$ defined by the formula

$$(S\varphi)(t) = x(t + \tau), \quad -\tau \leq t \leq 0,$$

where $x \colon [-\tau, \infty) \to \mathbb{R}$ is the unique solution of (11) which is continuous on $[-\tau, \infty)$, differentiable on $[0, \infty)$ and satisfies the initial value condition

$$x(t) = \varphi(t), \quad -\tau \le t \le 0.$$

We can describe the properties of equation (11) in terms of S. Namely, we shall say that a measure μ on C is invariant (ergodic) with respect to equation (11) if it is invariant (ergodic) under S.

Conjecture 1 ([18]). *For some positive values of the parameters γ, τ, n and β there exists on C a continuous probability measure which is ergodic and invariant with respect to equation (11).*

Delay Dynamics and Evolution of Densities

In examining the dynamical behavior of a system there are fundamentally two options available to the experimentalist.

1. In the first option s/he will examine the dynamical trajectories of individuals, be they fundamental particles in a cloud chamber or cells in a petri dish or animals in an ecological experiment. In this case the experimentalist may be interested in replicating the experiment many times, and building up a statistical description of the observed behavior under the assumption (among others) that the trajectory behavior will be replicated between trials given the same initial conditions.

2. In the second option this approach will be forsaken for one in which the evolving statistics of large populations are examined. This is, of course, most familiar in statistical mechanics, but is also important in many other areas. The advantage of this approach is that if one can understand the dynamics of density evolution, then many interesting statistical quantities can be computed, and the results compared with experimental results. Much of this material has been reviewed in Section Dynamical Systems and Evolution of Densities.

Which approach is taken is sometimes a matter of choice, but often dictated by the nature of the individual units being studied.

For systems in which the underlying dynamics are described by differential equations, or stochastic differential equations, or maps, there is a large *corpus* of methods that have been developed with which one can approach (in a modeling context) both of the types of data collection outlined above and the connection of that data to underlying dynamical systems theory.

However many problems in the physical, and especially the biological, sciences involve the dynamic behavior of individual entities whose dynamics involve significant delays. For problems like this, existing techniques to theoretically consider the evolution of densities are non-existent. Repeated attempts to think of ways to formulate the evolution of densities in the presence of dynamics with delays have failed in even the most elementary respects (e.g., defining the fundamental mathematical aspects of the problem). When dynamics are described by a differential delay equation of the form in equation (13) then we must consider what is likely to be measured. Figure 1 will aid in this.
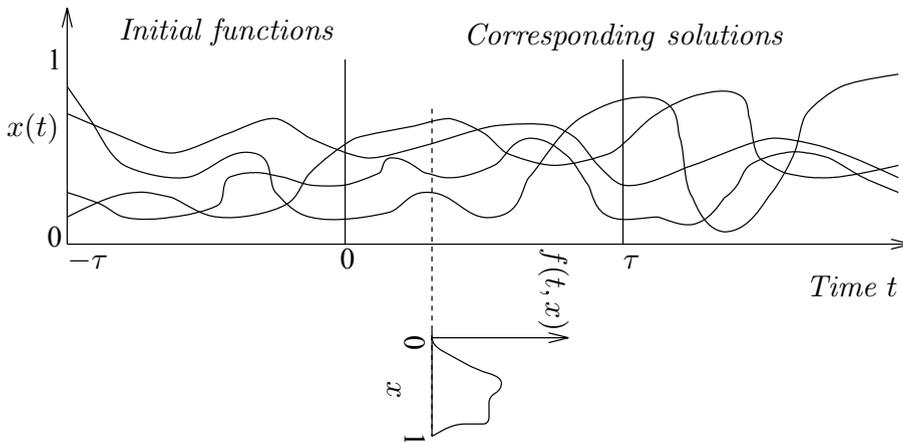

Figure 1. A schematic illustration of the connection between the evolution of an ensemble of initial functions and what would be measured in a laboratory. An ensemble of N initial functions on $[-\tau, 0]$ is allowed to evolve forward in time under the action of the delayed dynamics. At time t we sample the distribution of the values of x across all N trajectories and form an approximation to a density $f(t, x)$ given by ρ. Taken from [29] with permission.

Figure 1 shows a schematic depiction of what one would actually measure in an ensemble of units whose dynamic evolution is governed by a differential delay equation. We assume that there are N such units involved in our experiment, and that the experiment is started at time $t = 0$ with each of the N units having a history (= an initial function) on the interval $[-\tau, 0]$ preceding the start of the experiment. We let these N units evolve dynamically in time, and assume that we have a device able to record a histogram

approximation ρ to the density $f(t, x)$ of the distribution of the state variable x at time t.[1] Note that this measurement procedure is carried out at *successive* individual times and might be continuous.

Thus, what we *measure* is not unlike what we might measure in a system whose dynamics are evolving under the action of the system of ordinary differential equations (3). However, what we are able to *calculate* is far different.

To be more concrete, suppose we have a variable x evolving under the action of some dynamics described by a differential delay equation

$$\frac{dx}{dt} = \mathcal{F}(x(t), x(t - \tau)), \tag{13}$$

or the stochastic differential delay equation

$$dx = \mathcal{F}(x(t), x(t - \tau))dt + \sigma(x(t), x(t - \tau))dW(t), \tag{14}$$

with the initial condition $x(t) = \varphi(t)$, $t \in [-\tau, 0]$, where $W(t)$ is a standard Wiener process. Then we would like to know how some "density" f of the variable x will evolve in time, i.e., we would like to be able to write down an equation for an "unknown operator" $\mathcal{U}$

$$\mathcal{U}f = 0$$

Unfortunately we don't really know how to do this, and that's the whole point of this section. The reason that the problem is so difficult is embodied in equation (13) and the infinite dimensional nature of the problem because of the necessity of specifying the *initial function* $\varphi(t)$ for $t \in [-\tau, 0]$. However, we do have some clues about what $\mathcal{U}$ should look like in various limiting cases. For example, in equation (13) if $\tau \to 0$ then we should recover the normal Liouville equation (4) from $\mathcal{U}$. If $\tau \to 0$ in equation (14) then we should recover the Fokker–Planck equation (5).

Equation (13) might induce a semiflow $\{T_t\}_{t \geq 0}$ on a subset X of the space of continuous functions $C = C([-\tau, 0], \mathbb{R})$, which can be written as $x_t = T_t \varphi$ (see [7, 6]). In one sense, it would seem that the evolution of a density under the action of this semigroup would be given by an extension of equation (1)

$$\int_A P^t f(x) \, \mu(dx) = \int_{T_t^{-1}(A)} f(x) \, \mu(dx) \quad \text{for all measurable } A \subset X.$$

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[1]It sometimes might be the case that we would not measure ρ, but rather might have estimates of various moments of ρ like $< x >$, $< x^2 >$, etc.

This writing of the evolution of the density f under the action of the semigroup of Frobenius–Perron operators $P^t\colon L^1 \to L^1$ is, however, merely formal and serves to highlight the major problems that we face.

Namely the problem surfaces of:

1. what the measure μ on the space C is,

2. what is a density f on C,

3. what does it mean to do integration over subsets of C, and

4. how would you actually figure out what T_t^{-1} is?

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