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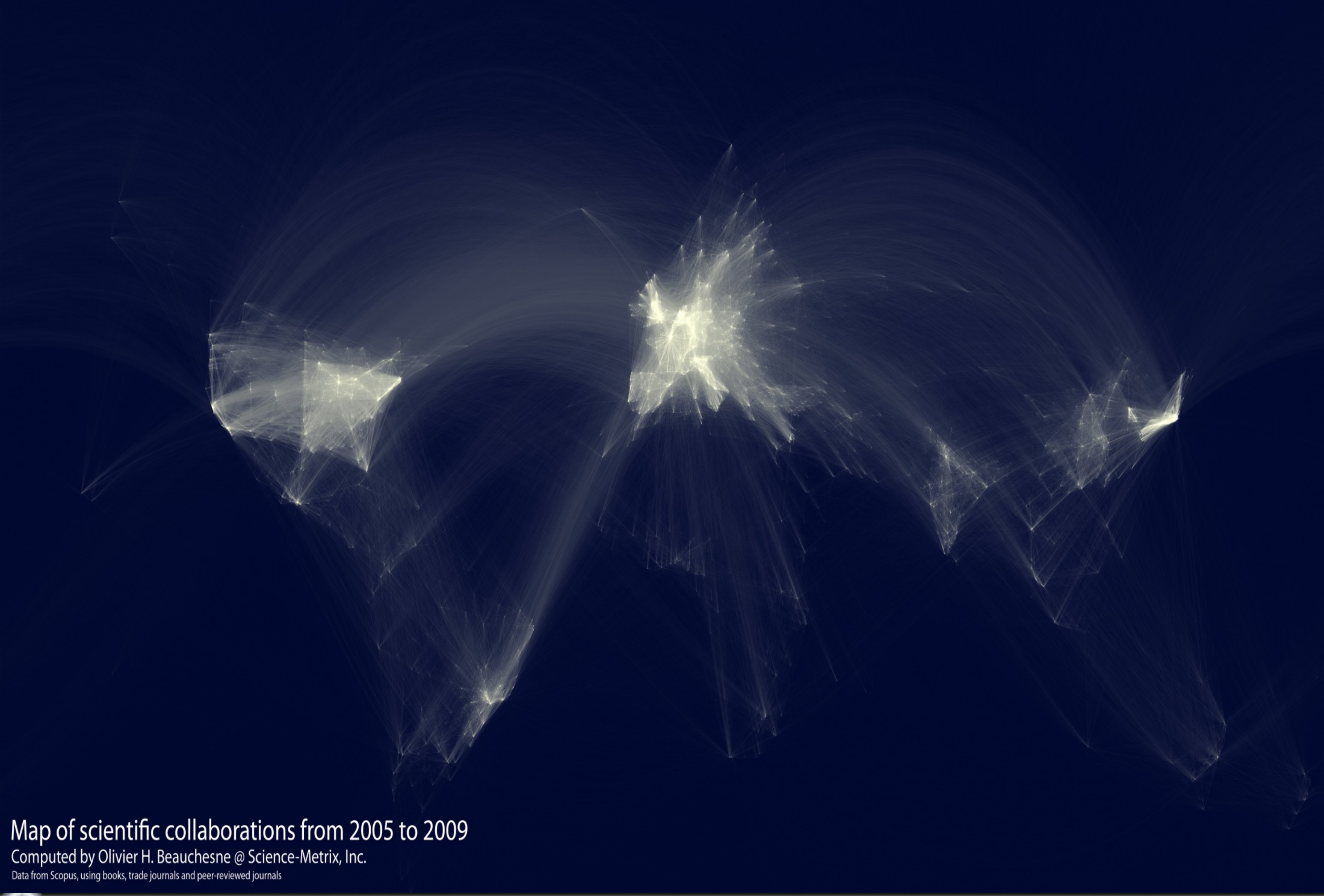

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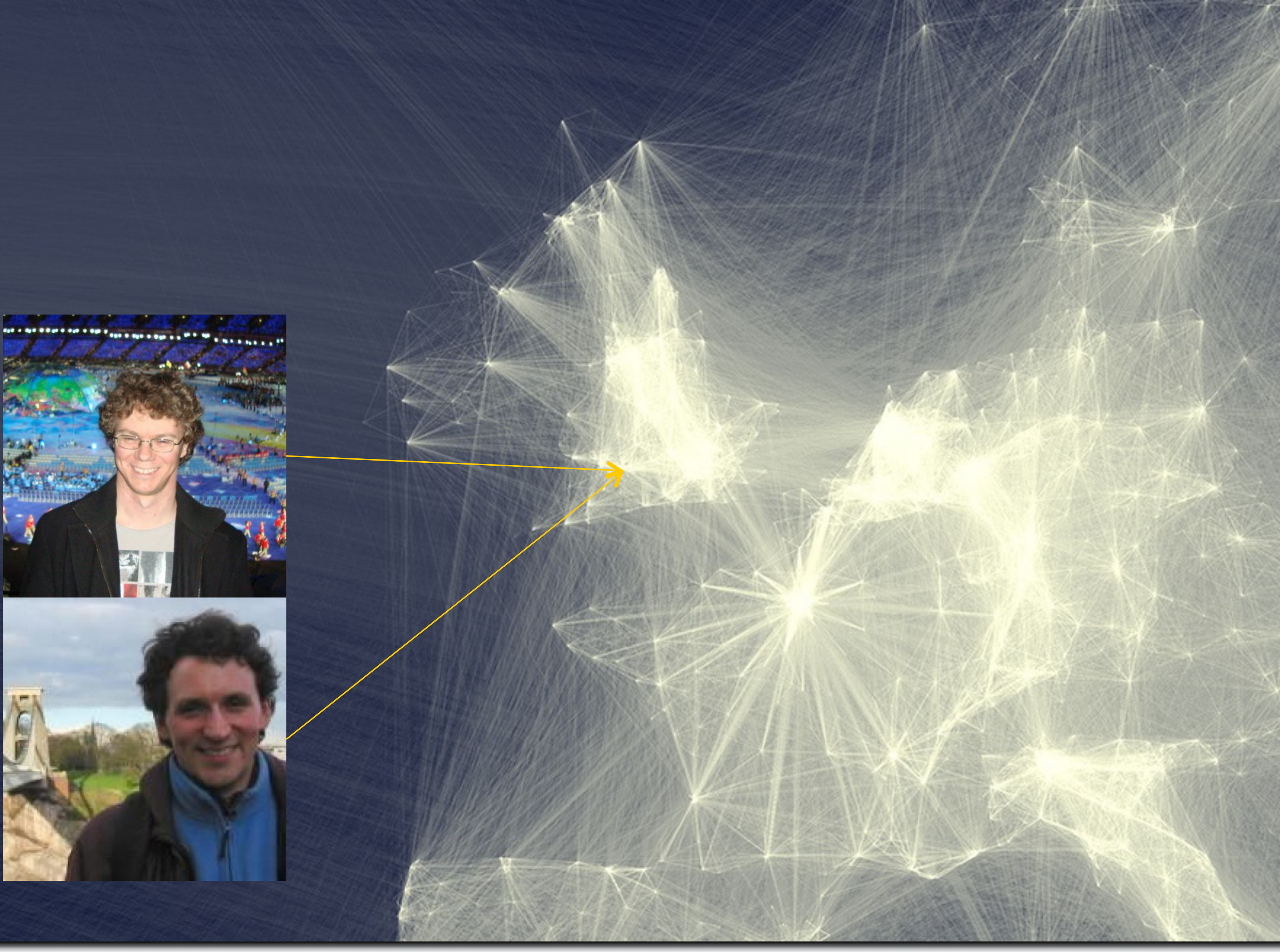

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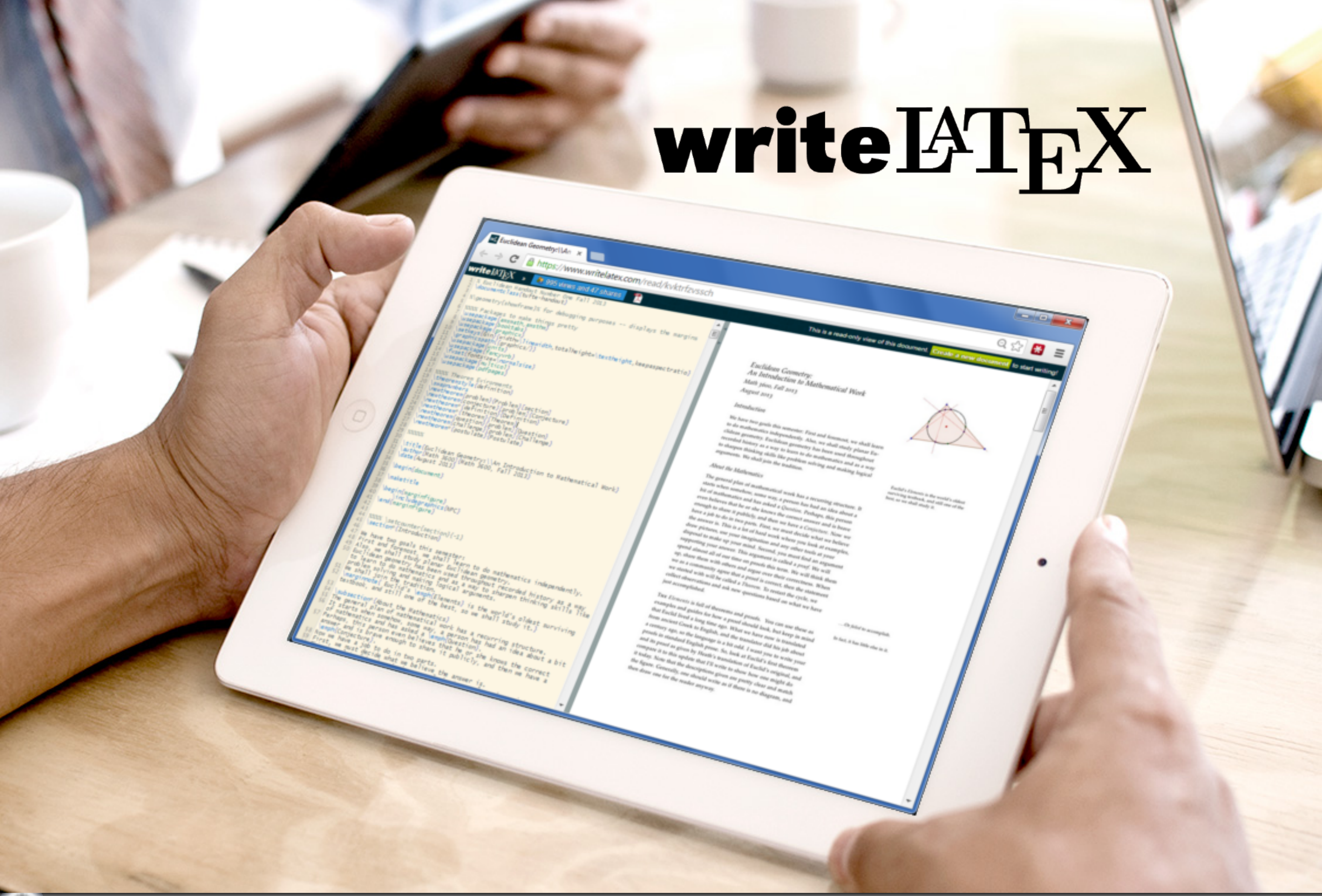

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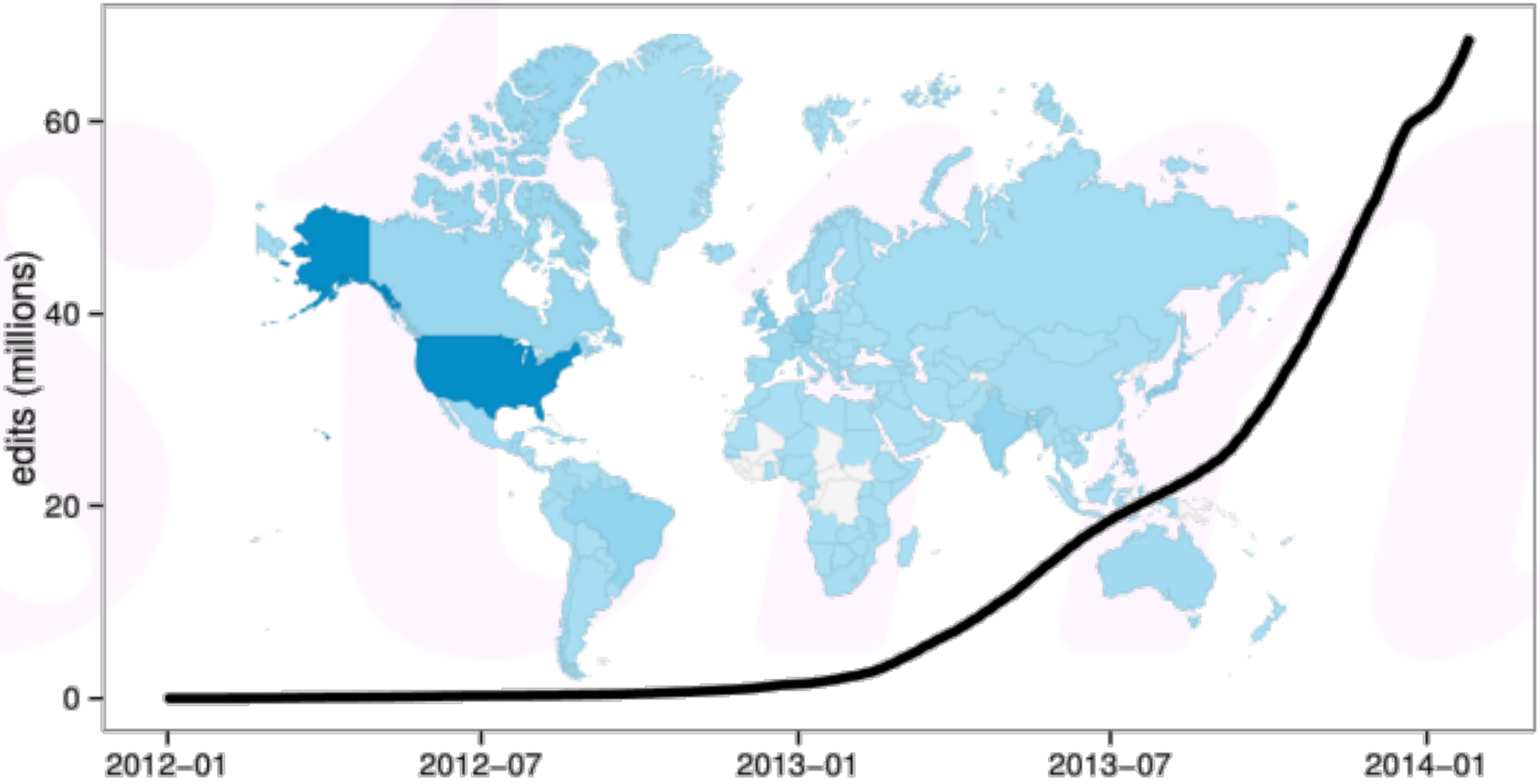

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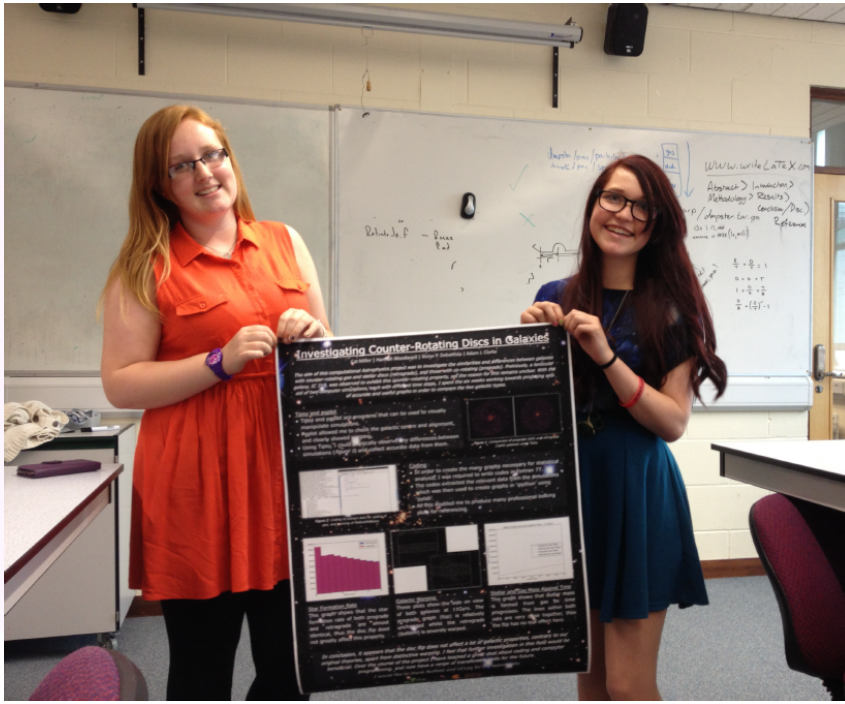

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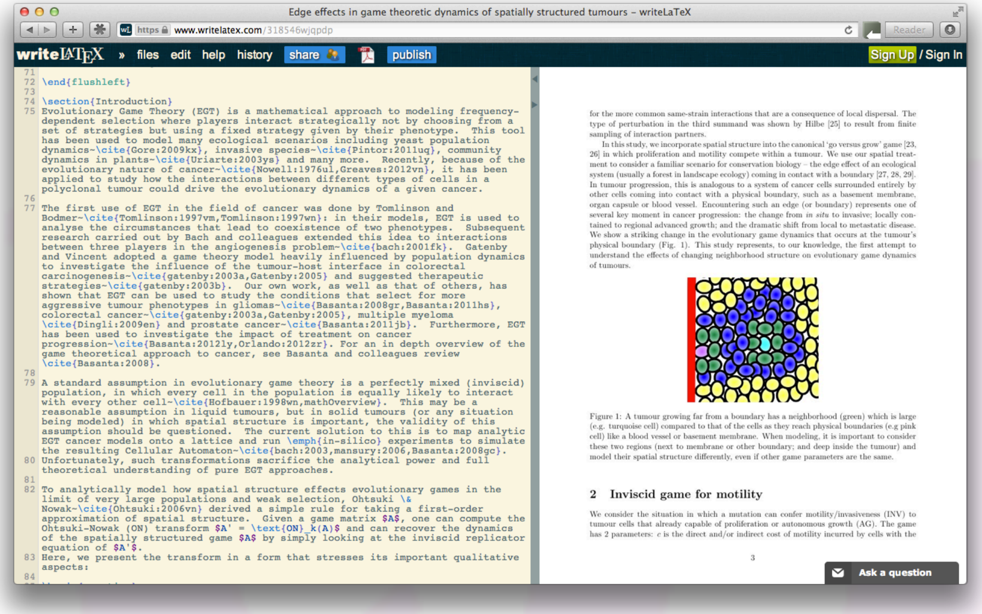

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\section{Introduction}
Evolutionary Game Theory (EGT) is a mathematical approach to modeling frequency-
dependent selection where players interact strategically not by choosing from a
set of strategies but using a fixed strategy given by their phenotype.  This tool
has been used to model many ecological scenarios including yeast population
dynamics~\cite{Gore:2009kx}, invasive species~\cite{Pintor:2011uq}, community
dynamics in plants~\cite{Uriarte:2003ys} and many more.  Recently, because of the
evolutionary nature of cancer~\cite{Nowell:1976ul,Greaves:2012vn}, it has been
applied to study how the interactions between different types of cells in a
polyclonal tumour could drive the evolutionary dynamics of a given cancer.

The first use of EGT in the field of cancer was done by Tomlinson and
Bodmer~\cite{Tomlinson:1997vm,Tomlinson:1997wn}: in their models, EGT is used to
analyse the circumstances that lead to coexistence of two phenotypes.  Subsequent
research carried out by Bach and colleagues extended this idea to interactions
between three players in the angiogenesis problem~\cite{bach:2001fk}.  Gatenby
and Vincent adopted a game theory model heavily influenced by population dynamics
to investigate the influence of the tumour-host interface in colorectal
carcinogenesis~\cite{gatenby:2003a,Gatenby:2005} and suggested therapeutic
strategies~\cite{gatenby:2003b}.  Our own work, as well as that of others, has
shown that EGT can be used to study the conditions that select for more
aggressive tumour phenotypes in gliomas~\cite{Basanta:2008gr,Basanta:2011hs},
colorectal cancer~\cite{gatenby:2003a,Gatenby:2005}, multiple myeloma
\cite{Dingli:2009en} and prostate cancer~\cite{Basanta:2011jb}.  Furthermore, EGT
has been used to investigate the impact of treatment on cancer
progression~\cite{Basanta:2012ly,Orlando:2012zr}. For an in depth overview of the
game theoretical approach to cancer, see Basanta and colleagues review
\cite{Basanta:2008}.

A standard assumption in evolutionary game theory is a perfectly mixed (inviscid)
population, in which every cell in the population is equally likely to interact
with every other cell~\cite{Hofbauer:1998wn,mathOverview}.  This may be a
reasonable assumption in liquid tumours, but in solid tumours (or any situation
being modeled) in which spatial structure is important, the validity of this
assumption should be questioned.  The current solution to this is to map analytic
EGT cancer models onto a lattice and run \emph{in-silico} experiments to simulate
the resulting Cellular Automaton~\cite{bach:2003,mansury:2006,Basanta:2008gc}.
Unfortunately, such transformations sacrifice the analytical power and full
theoretical understanding of pure EGT approaches.

To analytically model how spatial structure effects evolutionary games in the
limit of very large populations and weak selection, Ohtsuki \&
Nowak~\cite{Ohtsuki:2006vn} derived a simple rule for taking a first-order
approximation of spatial structure.  Given a game matrix $A$, one can compute the
Ohtsuki-Nowak (ON) transform $A' = \text{ON}_k(A)$ and can recover the dynamics
of the spatially structured game $A$ by simply looking at the inviscid replicator
equation of $A'$.
Here, we present the transform in a form that stresses its important qualitative
aspects:
```

for the more common same-strain interactions that are a consequence of local dispersal. The type of perturbation in the third summand was shown by Hilbe [25] to result from finite sampling of interaction partners.

In this study, we incorporate spatial structure into the canonical 'go versus grow' game [23, 26] in which proliferation and motility compete within a tumour. We use our spatial treatment to consider a familiar scenario for conservation biology – the edge effect of an ecological system (usually a forest in landscape ecology) coming in contact with a boundary [27, 28, 29]. In tumour progression, this is analogous to a system of cancer cells surrounded entirely by other cells coming into contact with a physical boundary, such as a basement membrane, organ capsule or blood vessel. Encountering such an edge (or boundary) represents one of several key moment in cancer progression: the change from *in situ* to invasive; locally contained to regional advanced growth; and the dramatic shift from local to metastatic disease. We show a striking change in the evolutionary game dynamics that occurs at the tumour's physical boundary (Fig. 1). This study represents, to our knowledge, the first attempt to understand the effects of changing neighborhood structure on evolutionary game dynamics of tumours.

Figure 1: A tumour growing far from a boundary has a neighborhood (green) which is large (e.g. turquoise cell) compared to that of the cells as they reach physical boundaries (e.g pink cell) like a blood vessel or basement membrane. When modeling, it is important to consider these two regions (next to membrane or other boundary; and deep inside the tumour) and model their spatial structure differently, even if other game parameters are the same.

2 Inviscid game for motility

We consider the situation in which a mutation can confer motility/invasiveness (INV) to tumour cells that already capable of proliferation or autonomous growth (AG). The game has 2 parameters: c is the direct and/or indirect cost of motility incurred by cells with the

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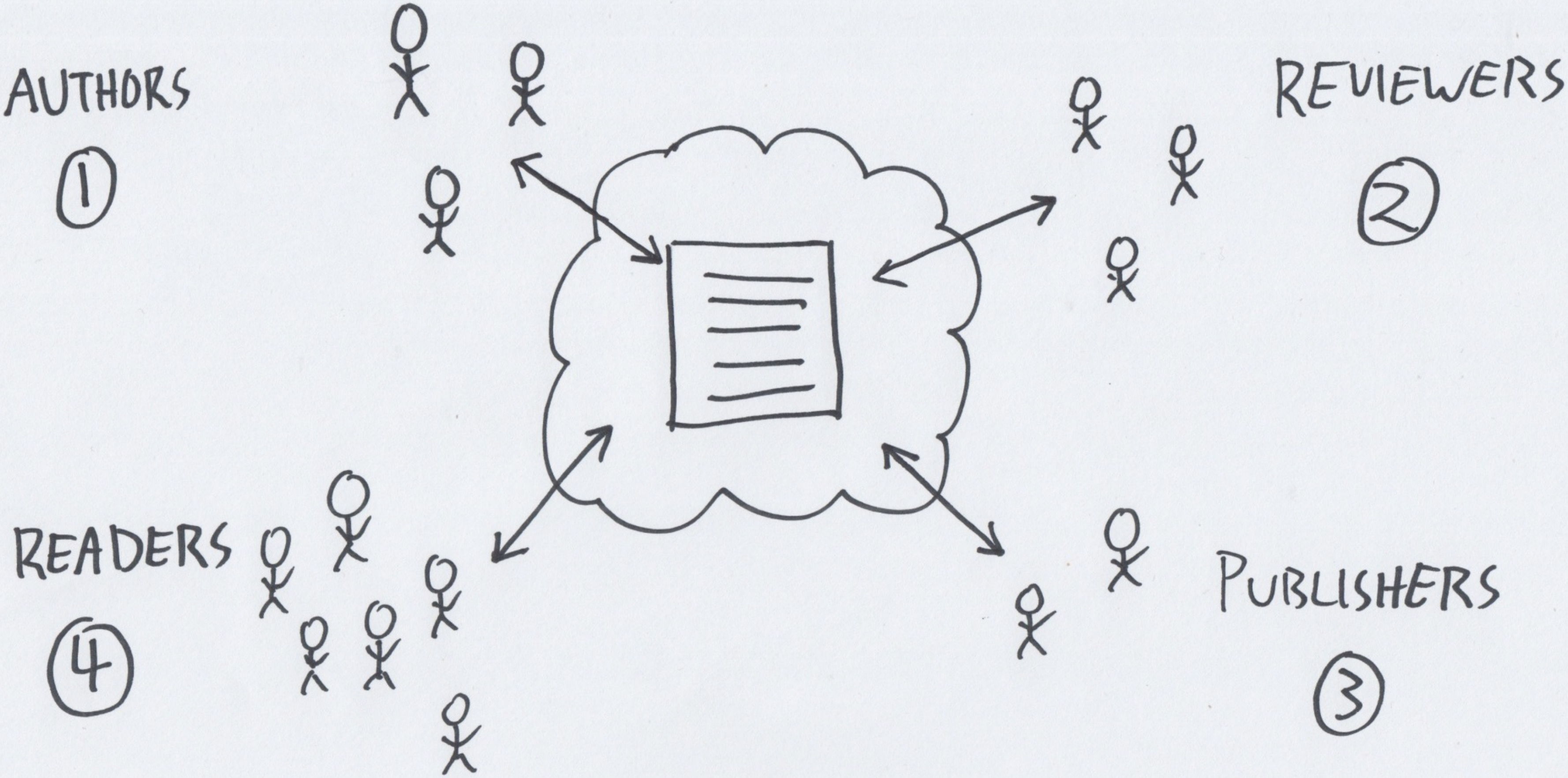
Researcher at McGill University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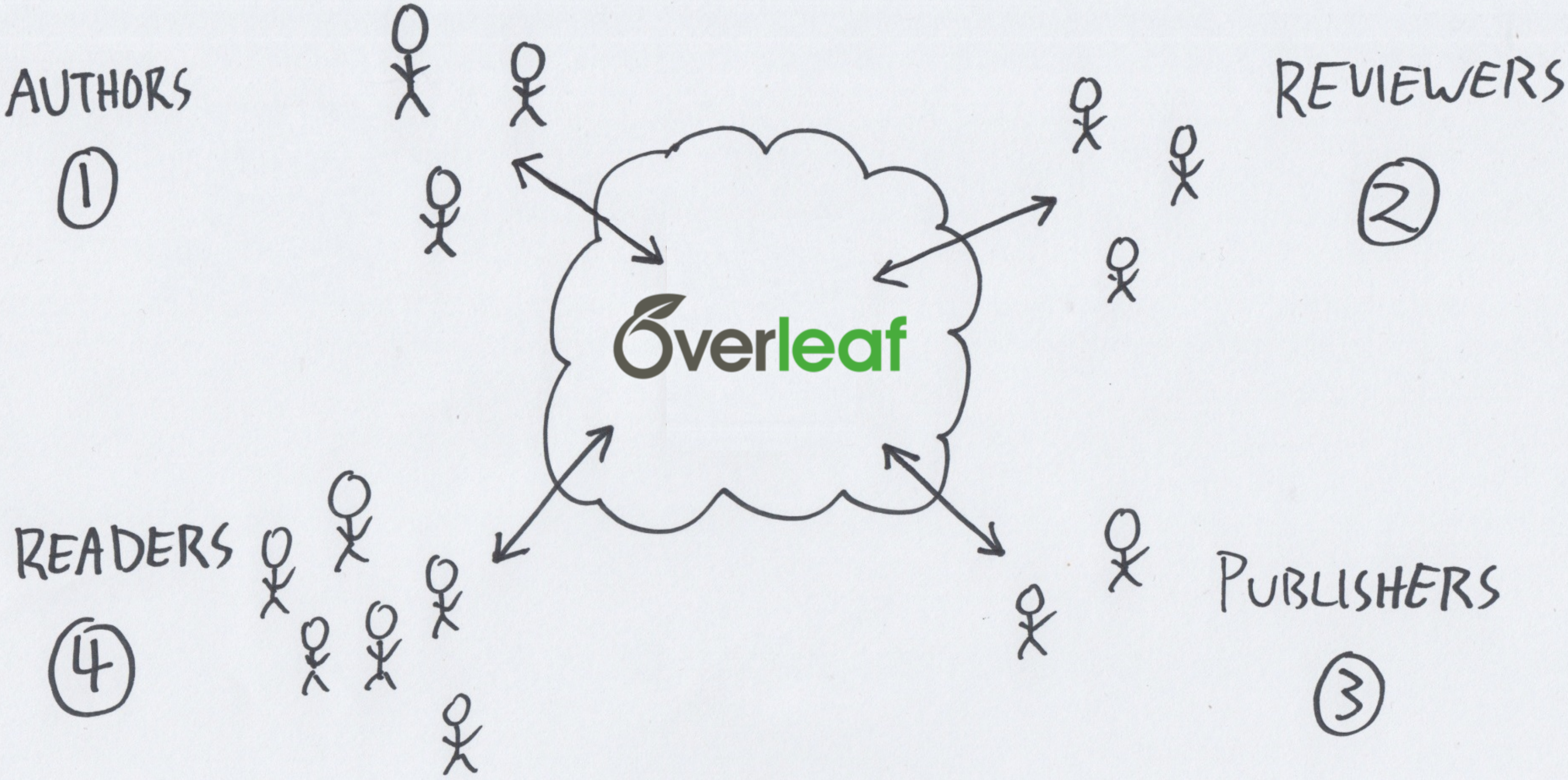

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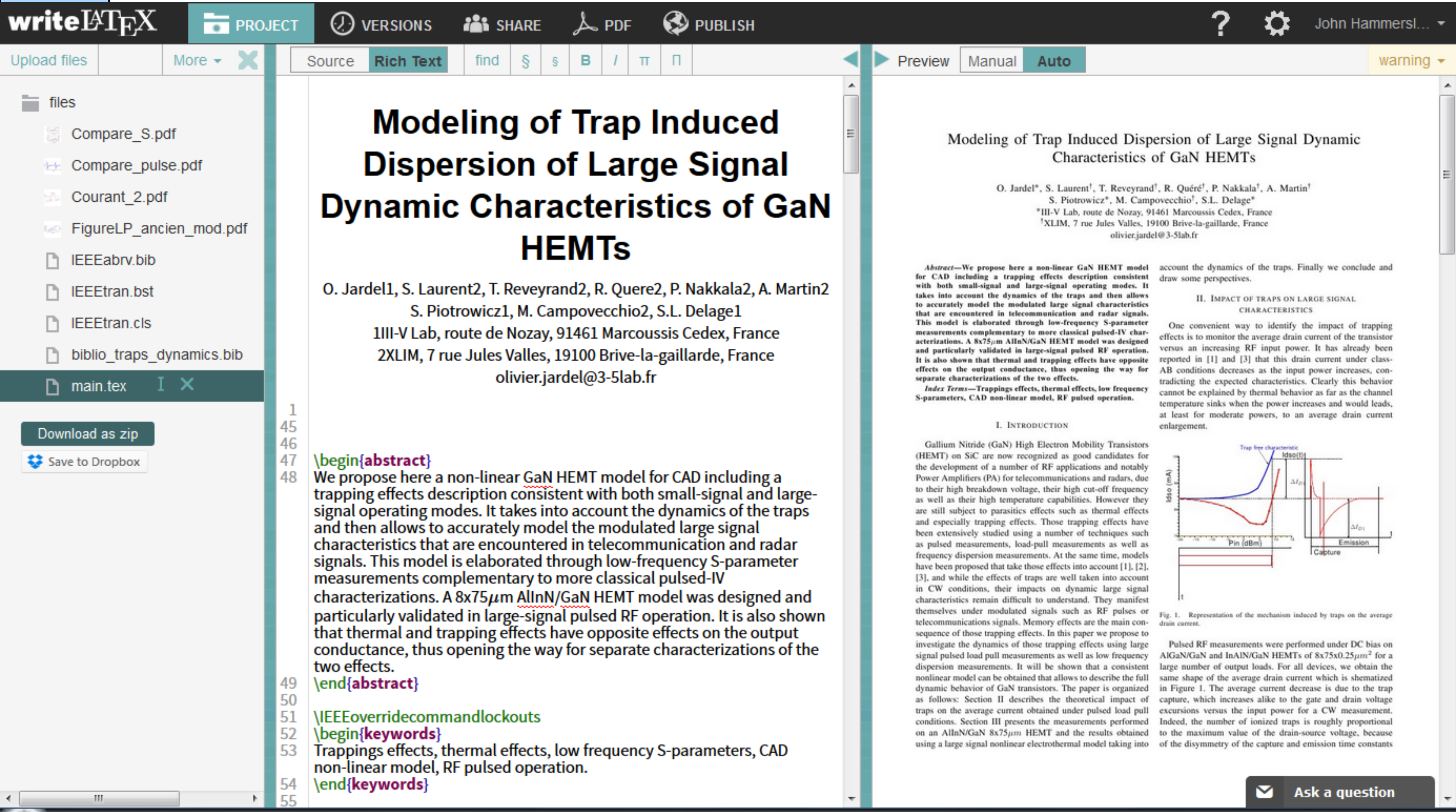

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We propose here a non-linear GaN HEMT model for CAD including a trapping effects description consistent with both small-signal and large-signal operating modes. It takes into account the dynamics of the traps and then allows to accurately model the modulated large signal characteristics that are encountered in telecommunication and radar signals. This model is elaborated through low-frequency S-parameter measurements complementary to more classical pulsed-IV characterizations. A 8x75μm AlInN/GaN HEMT model was designed and particularly validated in large-signal pulsed RF operation. It is also shown that thermal and trapping effects have opposite effects on the output conductance, thus opening the way for separate characterizations of the two effects.
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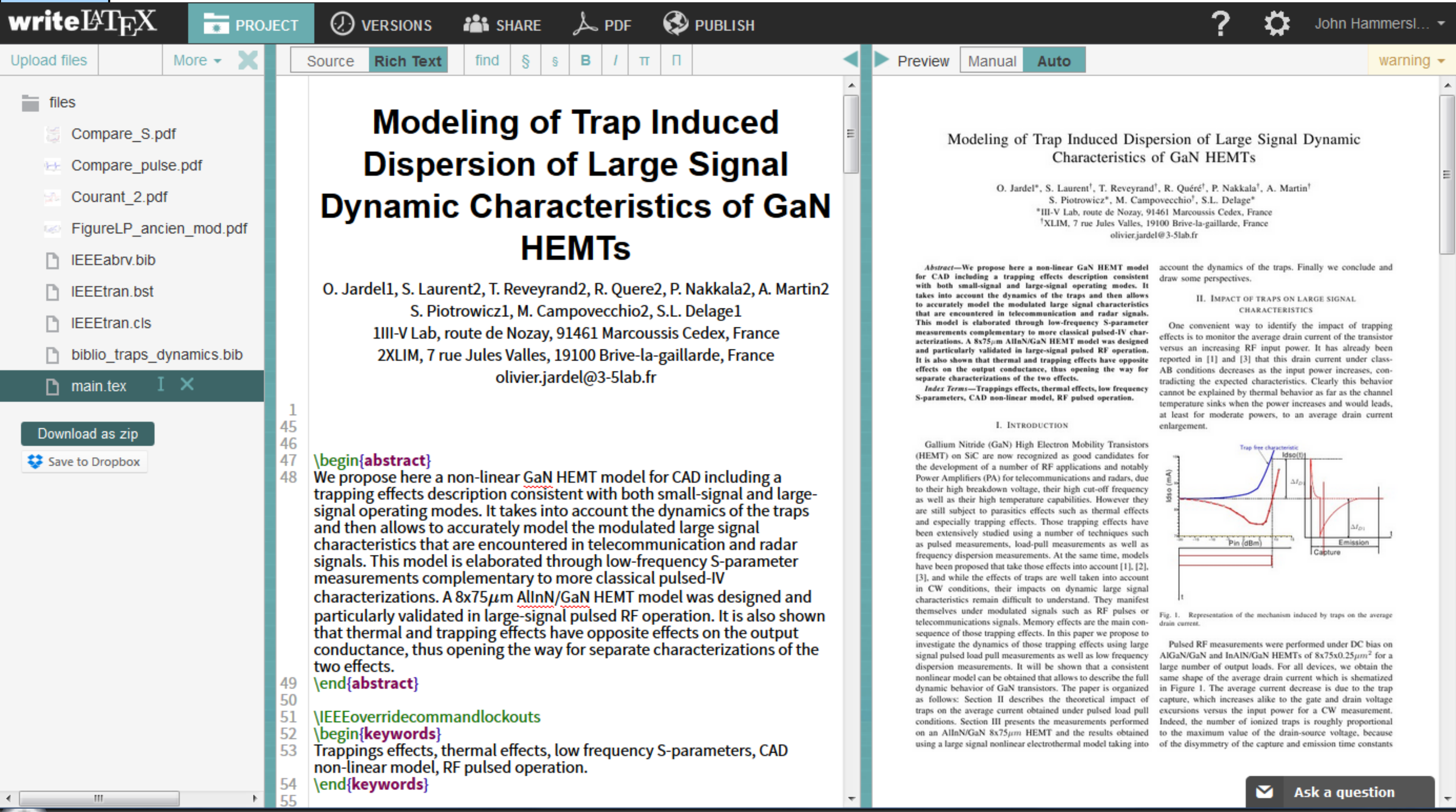

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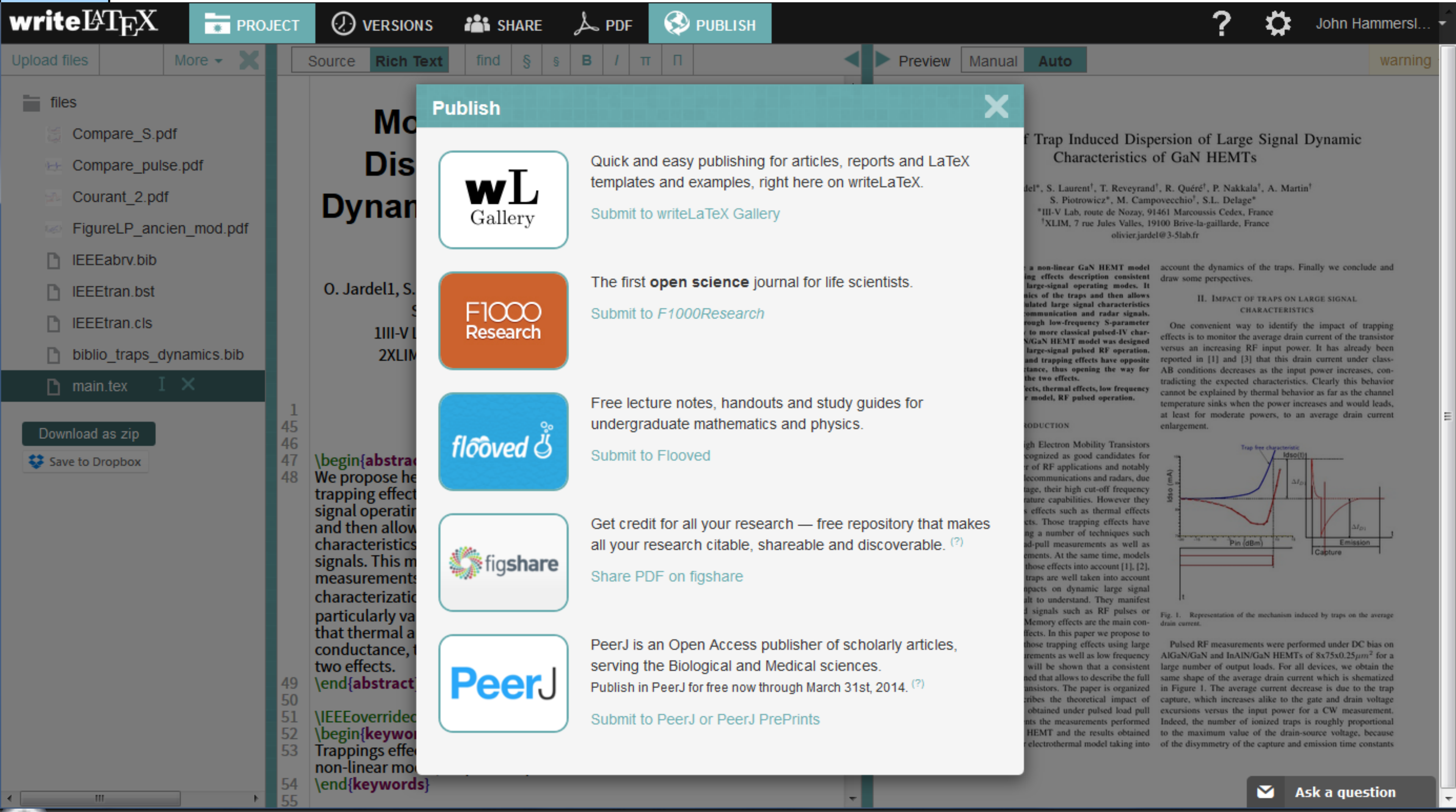

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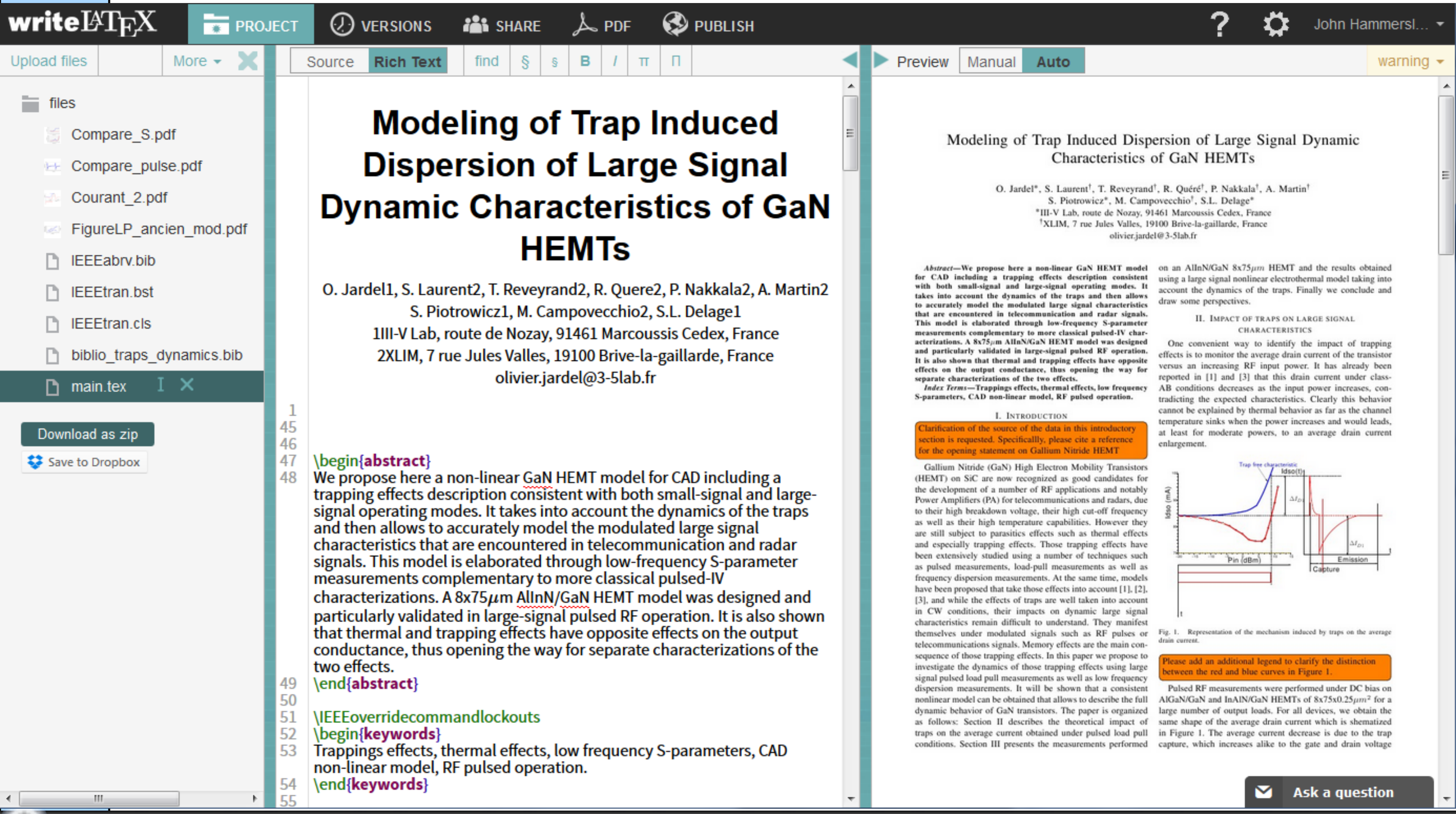

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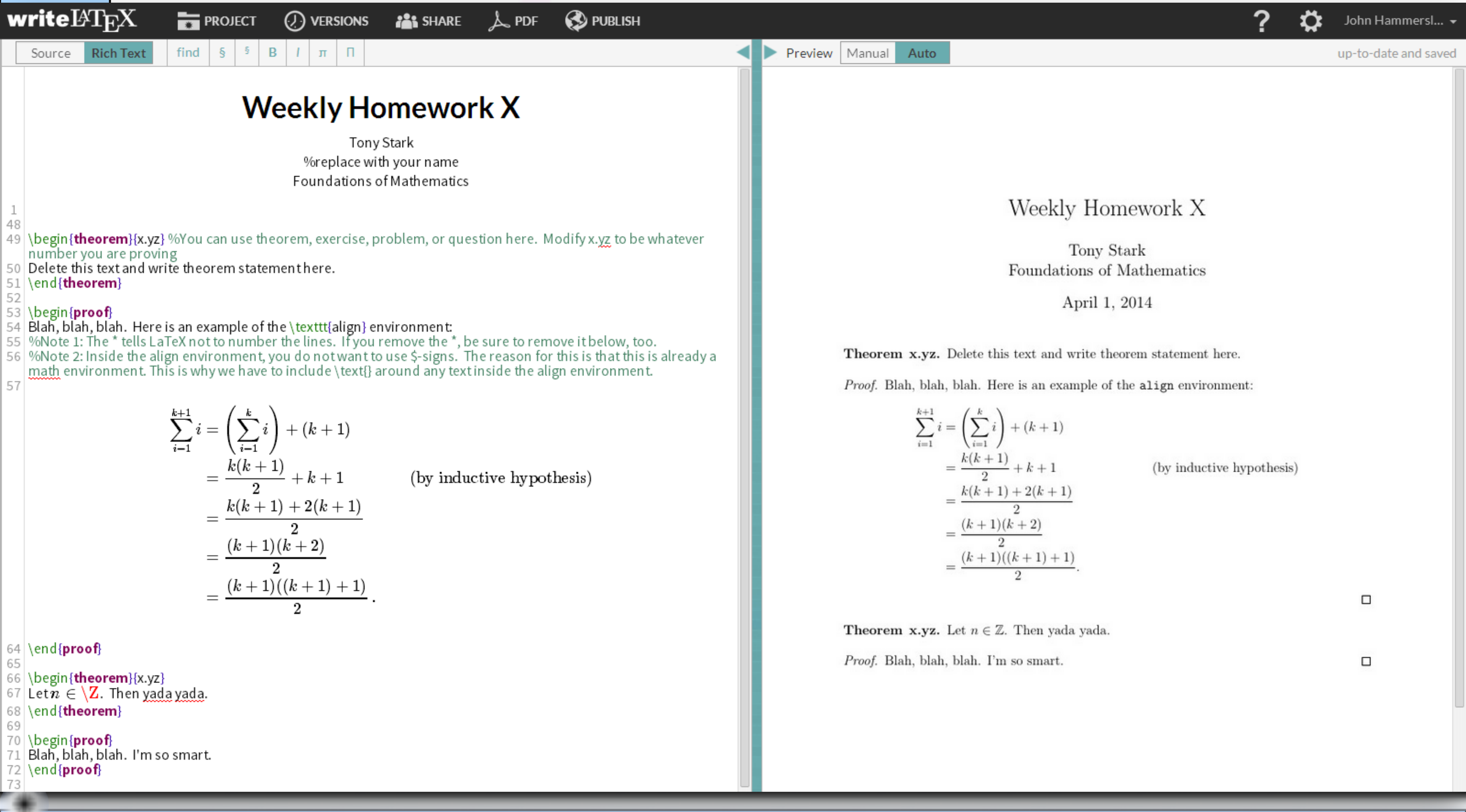

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\begin{proof}
Blah, blah, blah. Here is an example of the \texttt{align} environment:
%Note 1: The * tells LaTeX not to number the lines. If you remove the *, be sure to remove it below, too.
%Note 2: Inside the align environment, you do not want to use $-signs. The reason for this is that this is already a math environment. This is why we have to include \text{} around any text inside the align environment.
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$$\begin{aligned}\sum_{i=1}^{k+1} i &= \left(\sum_{i=1}^{k} i\right) + (k+1)\\ &= \frac{k(k+1)}{2} + k + 1 && \text{(by inductive hypothesis)}\\ &= \frac{k(k+1)+2(k+1)}{2}\\ &= \frac{(k+1)(k+2)}{2}\\ &= \frac{(k+1)((k+1)+1)}{2}.\end{aligned}$$

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\end{proof}

\begin{theorem}{x.yz}
Let $n \in$ \Z. Then yada yada.
\end{theorem}

\begin{proof}
Blah, blah, blah. I'm so smart.
\end{proof}
```

Weekly Homework X

Tony Stark
Foundations of Mathematics

April 1, 2014

Theorem x.yz. Delete this text and write theorem statement here.

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□

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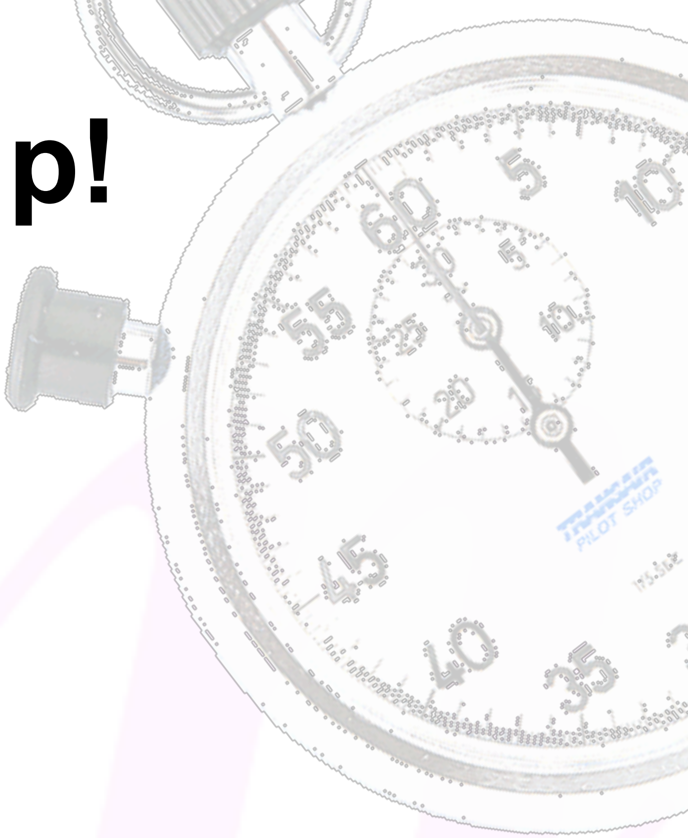

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