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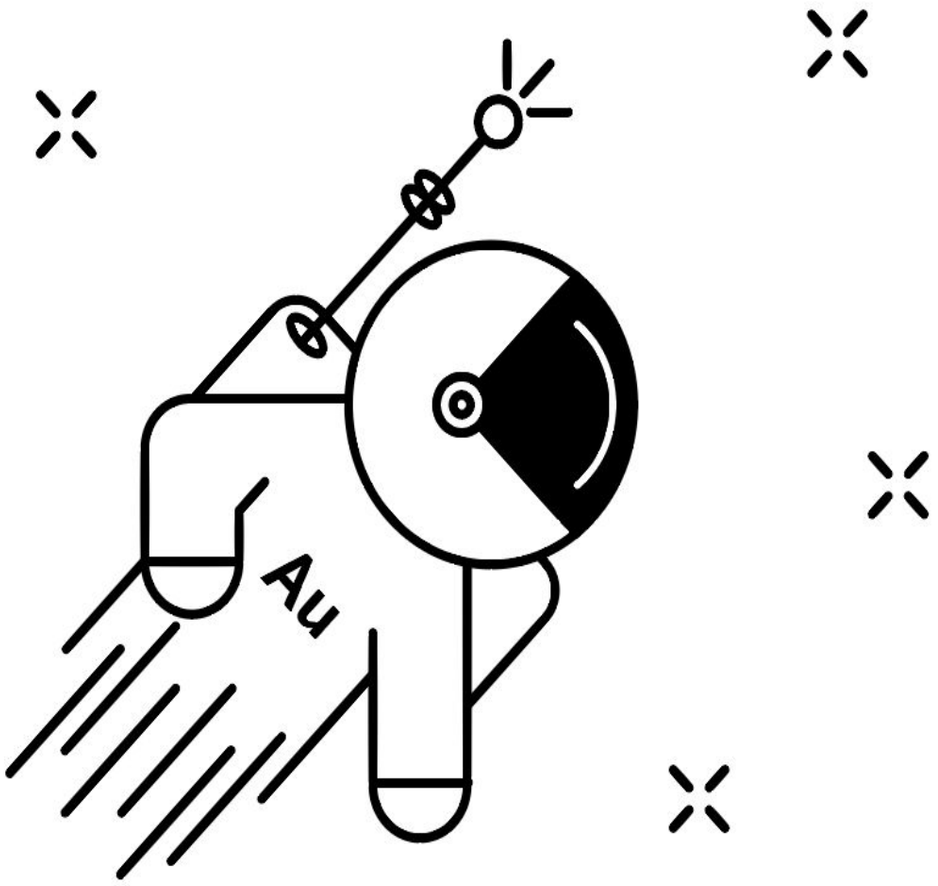

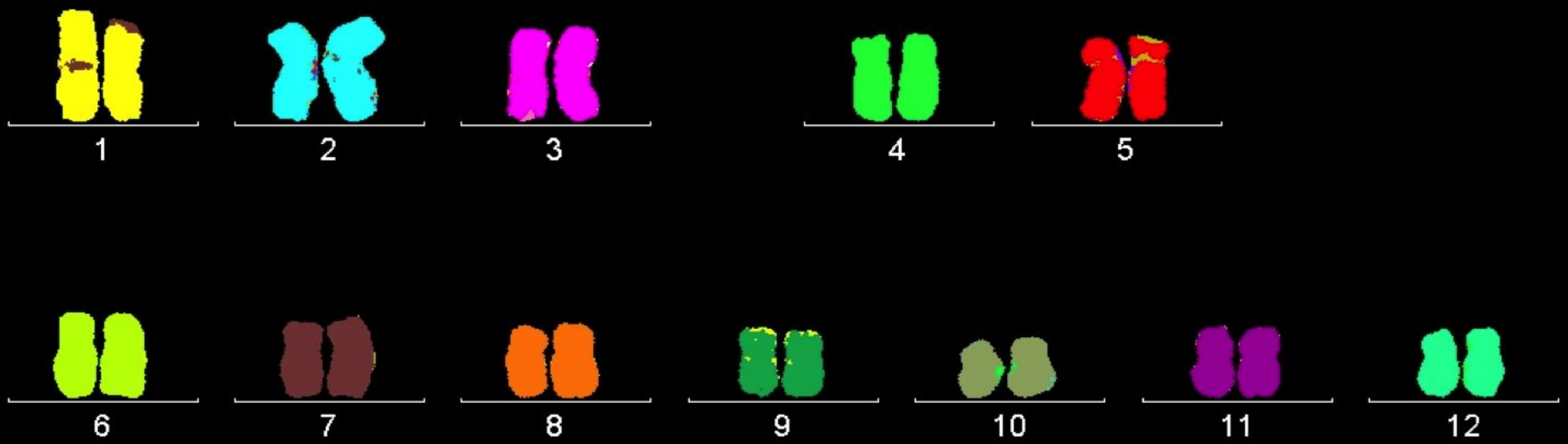
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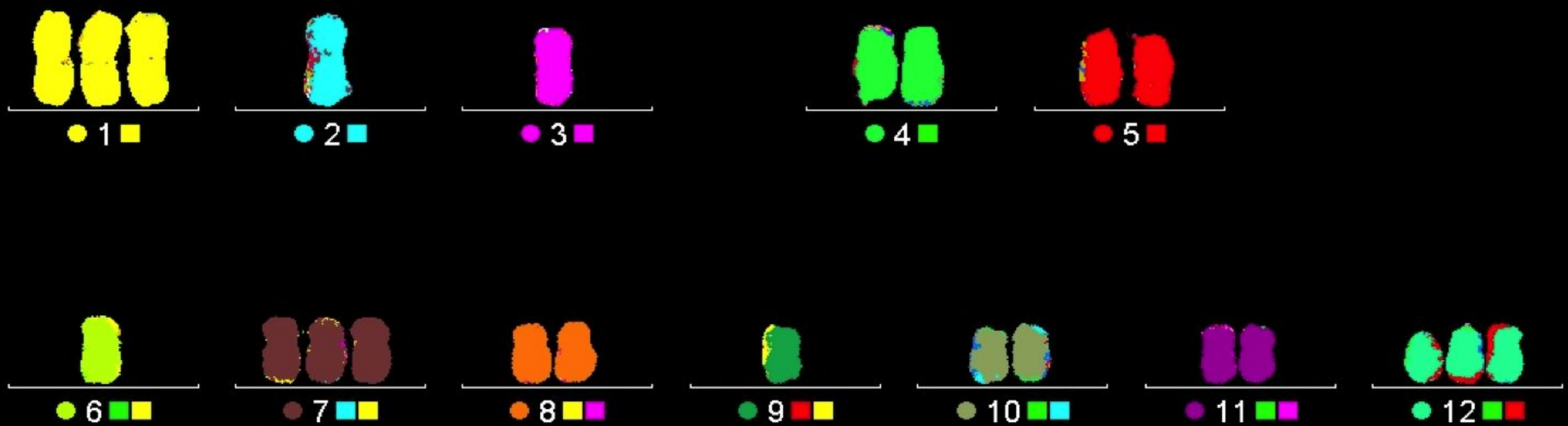
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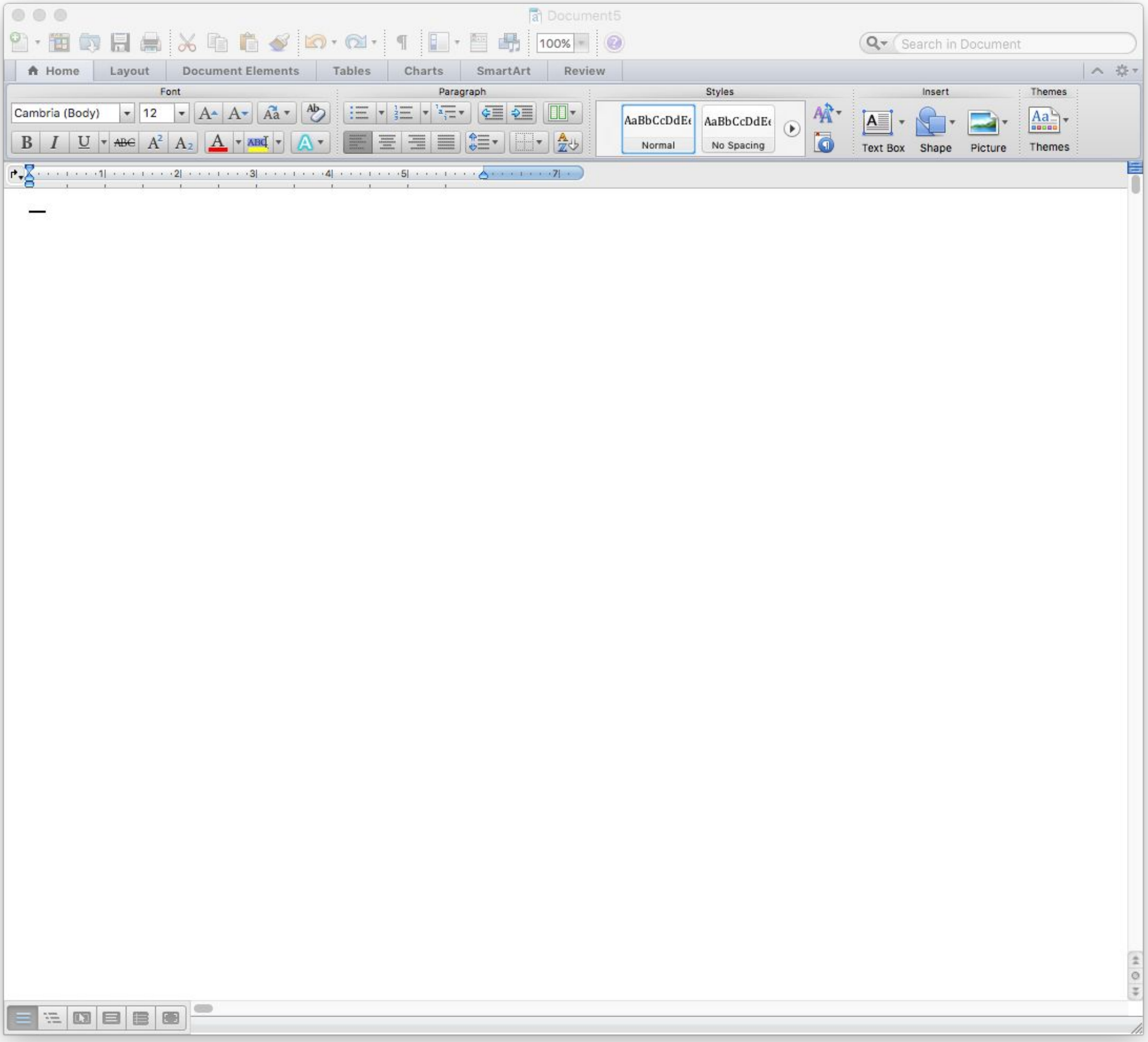
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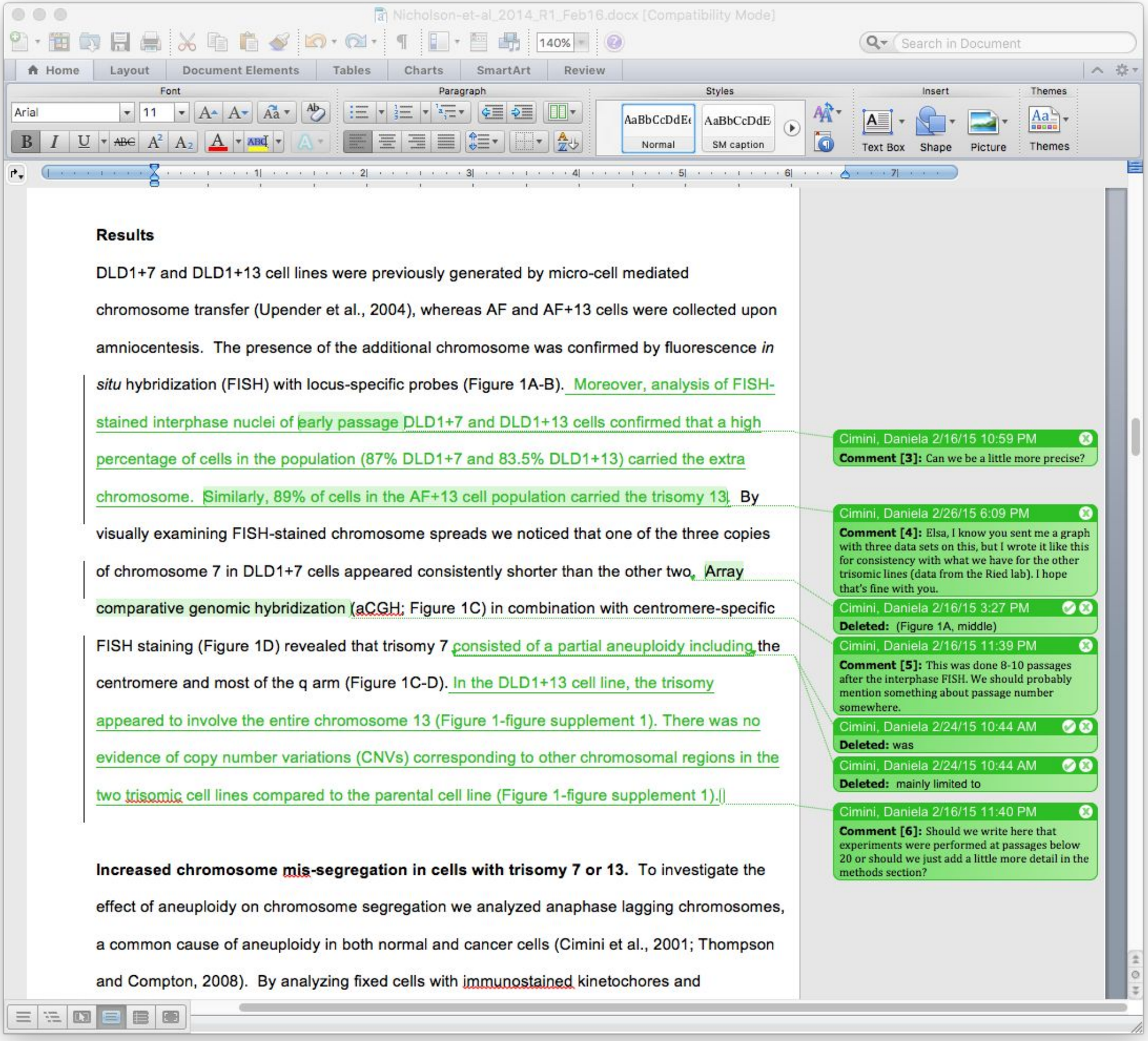
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Results
DLD1+7 and DLD1+13 cell lines were previously generated by micro-cell mediated chromosome transfer (Upender et al., 2004), whereas AF and AF+13 cells were collected upon amniocentesis. The presence of the additional chromosome was confirmed by fluorescence *in situ* hybridization (FISH) with locus-specific probes (Figure 1A-B). Moreover, analysis of FISH-stained interphase nuclei of early passage DLD1+7 and DLD1+13 cells confirmed that a high percentage of cells in the population (87% DLD1+7 and 83.5% DLD1+13) carried the extra chromosome. Similarly, 89% of cells in the AF+13 cell population carried the trisomy 13. By visually examining FISH-stained chromosome spreads we noticed that one of the three copies of chromosome 7 in DLD1+7 cells appeared consistently shorter than the other two. Array comparative genomic hybridization (aCGH; Figure 1C) in combination with centromere-specific FISH staining (Figure 1D) revealed that trisomy 7 consisted of a partial aneuploidy including the centromere and most of the q arm (Figure 1C-D). In the DLD1+13 cell line, the trisomy appeared to involve the entire chromosome 13 (Figure 1-figure supplement 1). There was no evidence of copy number variations (CNVs) corresponding to other chromosomal regions in the two trisomic cell lines compared to the parental cell line (Figure 1-figure supplement 1).
Increased chromosome mis-segregation in cells with trisomy 7 or 13. To investigate the effect of aneuploidy on chromosome segregation we analyzed anaphase lagging chromosomes, a common cause of aneuploidy in both normal and cancer cells (Cimini et al., 2001; Thompson and Compton, 2008). By analyzing fixed cells with immunostained kinetochores and
Cimini, Daniela 2/16/15 10:59 PM
Comment [3]: Can we be a little more precise?
Cimini, Daniela 2/26/15 6:09 PM
Comment [4]: Elsa, I know you sent me a graph with three data sets on this, but I wrote it like this for consistency with what we have for the other trisomic lines (data from the Ried lab). I hope that's fine with you.
Cimini, Daniela 2/16/15 3:27 PM
Deleted: (Figure 1A, middle)
Cimini, Daniela 2/16/15 11:39 PM
Comment [5]: This was done 8-10 passages after the interphase FISH. We should probably mention something about passage number somewhere.
Cimini, Daniela 2/24/15 10:44 AM
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Cimini, Daniela 2/24/15 10:44 AM
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Cimini, Daniela 2/16/15 11:40 PM
Comment [6]: Should we write here that experiments were performed at passages below 20 or should we just add a little more detail in the methods section?

cimini, me, Elsa (9)	Inbox	Fwd: eLife decision: 06-10-2014-RA-eLife-05068R1 - , Josh Nicholson wrote: > >> Here are my edits on the MS. I think		4/22/15
Daniela .. Elsa (9), Draft	Inbox	eLife reviews - Dear Daniela and dear Josh, sorry for the delayed reply. I included my comments over Daniela's		11/25/14
Daniela, me (4)	Inbox	Manuscript - , Joshua Nicholson wrote: > Hi Daniela, > > Bad news: All the N1 vector transfection movies and some of t		8/5/14
me		Experiments - done already. As you know we already have an MS ready but it will undoubtedly need some work before resubmis		2/19/14
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editorial .. cimini, me (7)	Inbox	eLife decision: 06-10-2014-RA-eLife-05068R2 - Subject: eLife decision: 06-10-2014-RA-eLife-05068R2 > To: cimini@vt.edu	📎	5/2/15
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RESEARCH ARTICLE

Chromosome mis-segregation and cytokinesis failure in trisomic human cells

Joshua M Nicholson[1,2], Joana C Macedo[3,4,5], Aaron J Mattingly[1†], Darawalee Wangsa[6], Jordi Camps[6‡], Vera Lima[7], Ana M Gomes[3], Sofia Dória[7], Thomas Ried[6], Elsa Logarinho[3,4,5]*, Daniela Cimini[1,2]*

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Abstract Cancer cells display aneuploid karyotypes and typically mis-segregate chromosomes at high rates, a phenotype referred to as chromosomal *in*stability (CIN). To test the effects of aneuploidy on chromosome segregation and other mitotic phenotypes we used the colorectal cancer cell line DLD1 (2n = 46) and two variants with trisomy 7 or 13 (DLD1+7 and DLD1+13), as well as euploid and trisomy 13 amniocytes (AF and AF+13). We found that trisomic cells displayed higher rates of chromosome mis-segregation compared to their euploid counterparts. Furthermore, cells with trisomy 13 displayed a distinctive cytokinesis failure phenotype. We showed that up-regulation of SPG20 expression, brought about by trisomy 13 in DLD1+13 and AF+13 cells, is sufficient for the cytokinesis failure phenotype. Overall, our study shows that aneuploidy can induce chromosome mis-segregation. Moreover, we identified a trisomy 13-specific mitotic phenotype that is driven by up-regulation of a gene encoded on the aneuploid chromosome.
DOI: 10.7554/eLife.05068.001

Introduction

Aneuploidy, an abnormal number of chromosomes, is a leading cause of mis-carriage and birth defects in humans (***Nagaoka et al., 2012***). In the vast majority of cases, this is due to errors occurring in the oocyte (***Nagaoka et al., 2012***). However, aneuploidy can also arise in somatic cells, and a number of studies have reported age-dependent increases in aneuploidy in human peripheral blood lymphocytes (***Nowinski et al., 1990***; ***Carere et al., 1999***; ***Leopardi et al., 2002***). Moreover, aneuploidy was recognized as a common feature of cancer cells already a century ago (***Boveri, 1914***, ***2008***), and a causal role of aneuploidy in carcinogenesis is currently largely acknowledged (reviewed in [***Pavelka et al., 2010a***; ***Nicholson and Cimini, 2011***]). In addition to being aneuploid, cancer cells typically display high rates of chromosome mis-segregation, a phenomenon termed chromosomal *in*stability (CIN) (***Lengauer et al., 1997***; ***Bakhoum et al., 2014***). The observation that even mosaic aneuploidy can cause severe physical and cognitive developmental defects (***Biesecker and Spinner, 2013***) indicates that aneuploidy has pleiotropic deleterious effects. This idea is further supported by a number of experimental observations: first, knocking down spindle assembly checkpoint genes, which results in high rates chromosome mis-

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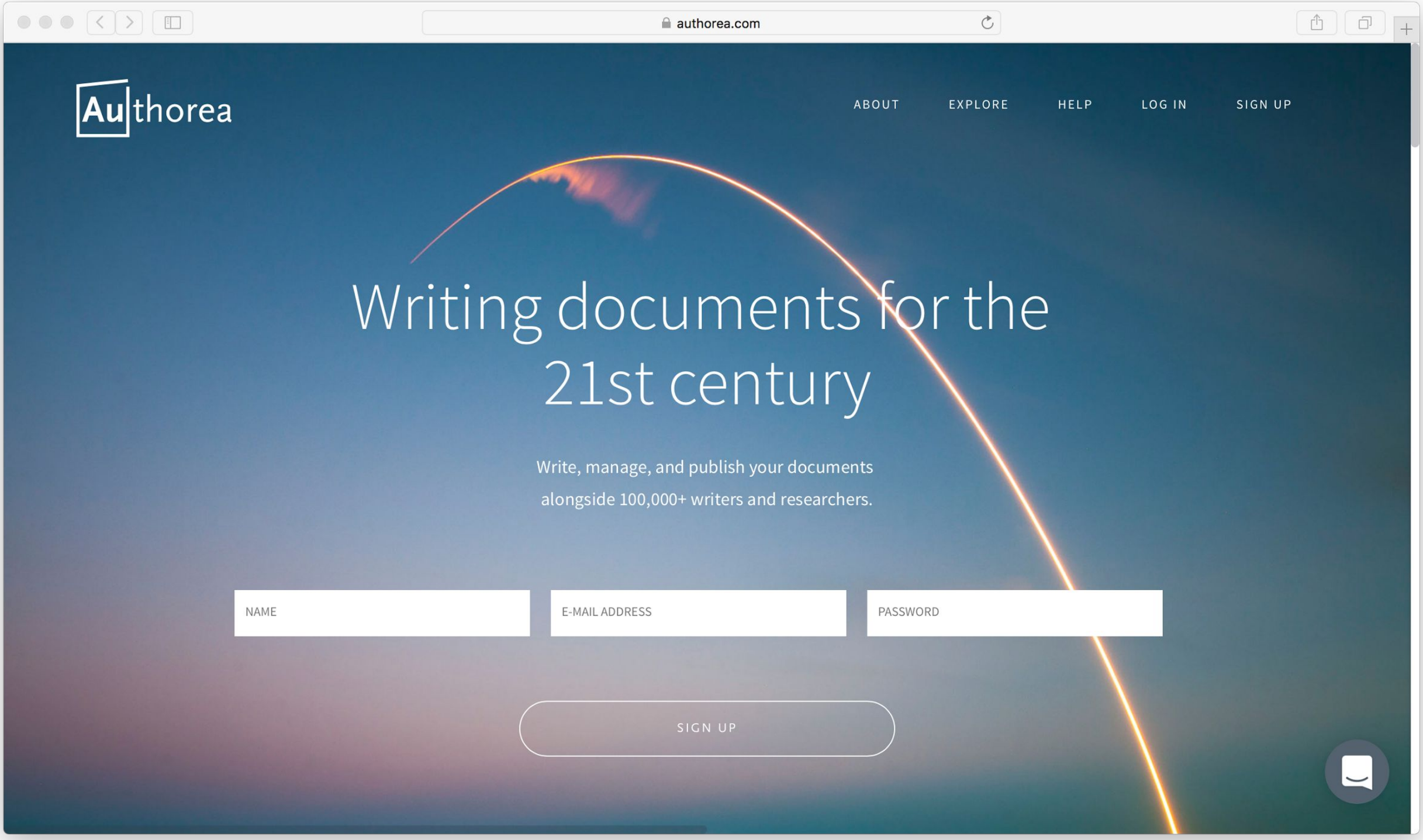
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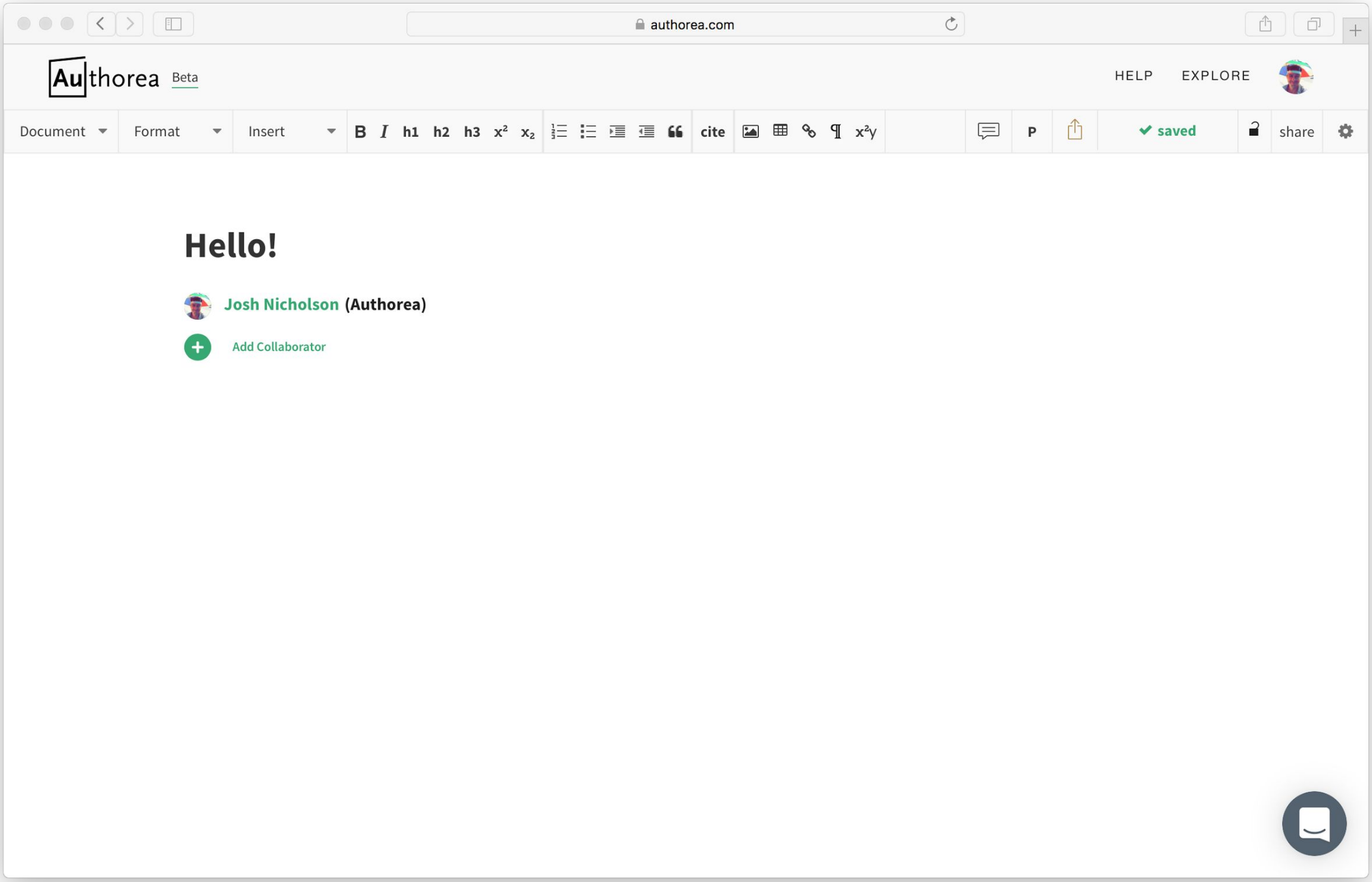
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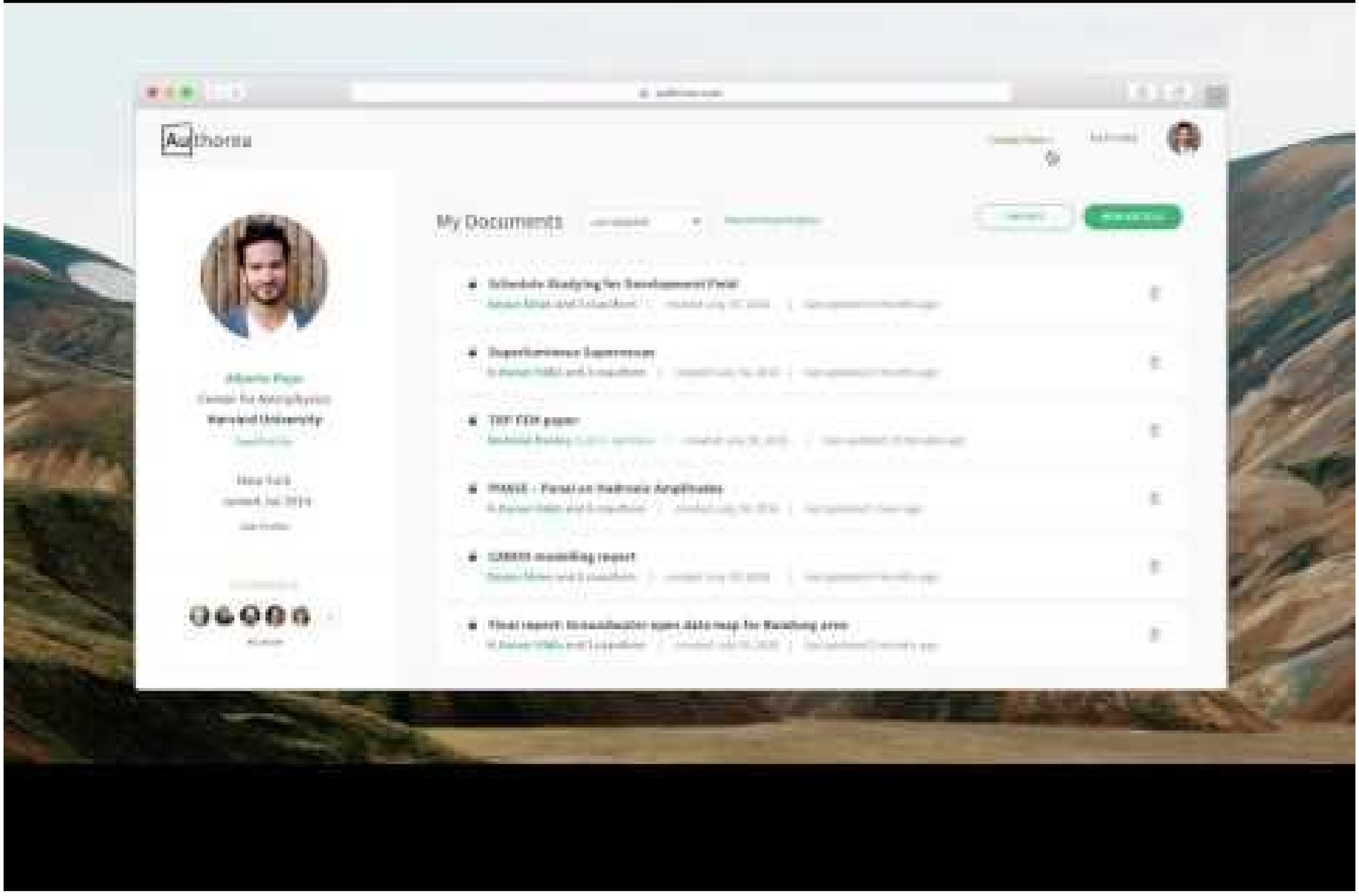
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The arXiv of the future will not look like the arXiv

Authorea preprint 06/08/2017 DOI: 10.22541/au.149693987.70506124

 **Alberto Pepe** **(Authorea)**

 **Matteo Cantiello** **(Simons Foundation)**

 Josh Nicholson **(Authorea)**

Abstract

The arXiv is the most popular preprint repository in the world. Since its inception in 1991, the arXiv has allowed researchers to freely share publication-ready articles prior to formal peer review. The growth and the popularity of the arXiv emerged as a result of new technologies that made document creation and dissemination easy, and cultural practices where collaboration and data sharing were dominant. The arXiv represents a unique place in the history of research communication and the Web itself, however it has arguably changed very little since its creation. Here we look at the strengths and weaknesses of arXiv in an effort to identify what possible improvements can be made based on new technologies not previously available. Based on this, we argue that a modern arXiv might in fact not look at all like the arXiv of today.

Introduction

The arXiv, pronounced "archive", is the most popular preprint repository in the world. Started in 1991 by physicist Paul Ginsparg, the arXiv allows researchers to freely share publication-ready articles prior to formal peer review and publication. Today, the arXiv publishes over 10,000 articles each month from high-energy physics, computer science, quantitative biology, statistics, quantitative finance, and others (see Fig 1). The early success of arXiv stems from the introduction of new technological advances paired to a

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The topic of automation replacing human jobs has been receiving a great deal of media attention in recent months. In January, the McKinsey Global Institute (Manyika et al., 2017) published a report stating 51% of job tasks (not jobs) could be automated with current technologies. The topic of 'big data' and algorithms was also briefly discussed on the Rasch listserv last year and offered a great deal of food-for-thought regarding the future of psychometrics in particular.

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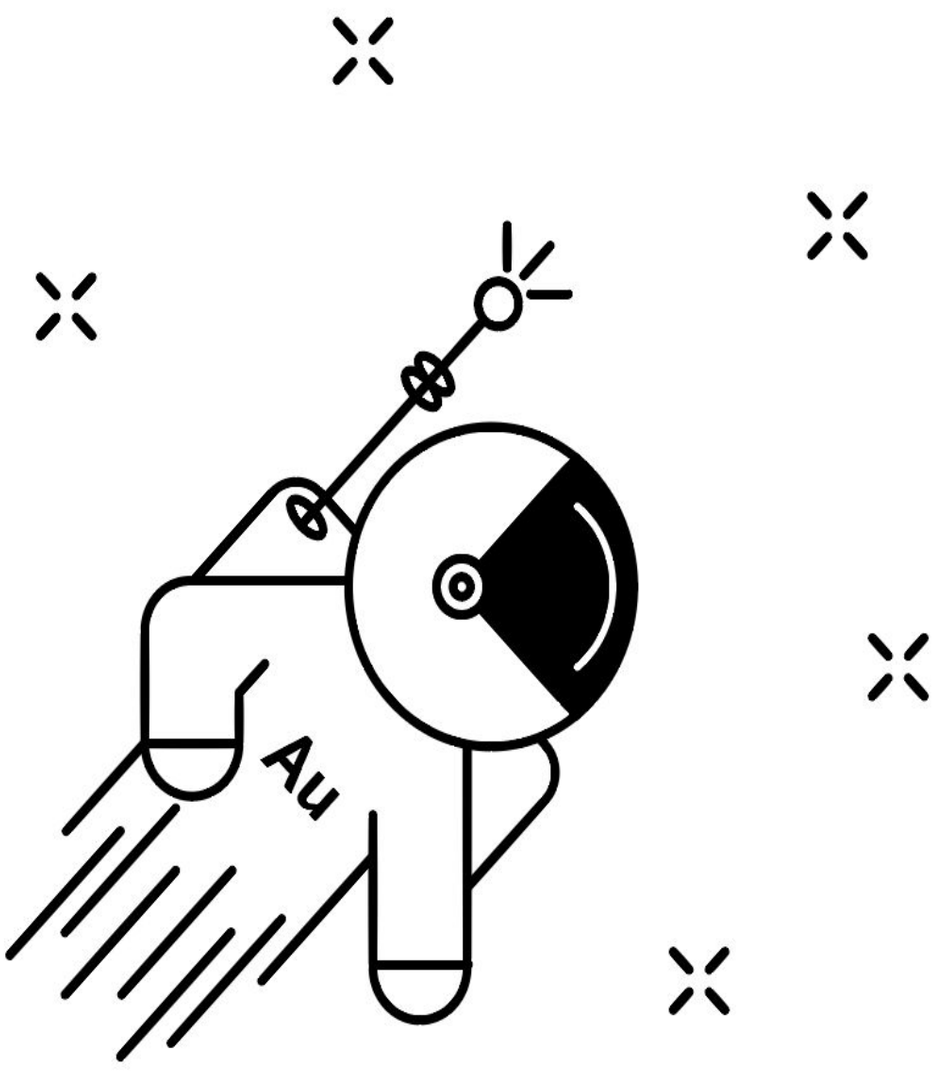

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