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PART IV

THE FUTURE OF COLLABORATIONS

25

COLLABORATION USING OPEN NOTEBOOK SCIENCE IN ACADEMIA

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25.1 INTRODUCTION

Technology has a profound effect on how scientists can communicate with each other. This affects how quickly science can progress and what kinds of collaboration are possible. Although the printing press and the subsequent establishment of scientific journals dramatically increased the ability of researchers to disseminate their results and ideas, close collaborations between geographically separated individuals had to await the availability of telecommunication technologies, particularly the development of the Internet.

Today, the ubiquity of sophisticated and easy-to-use tools to exchange information is enabling the creation of a "shared presence" between people, regardless of their geographical location. Researchers can share not only their data but also details regarding how they processed their data, their interpretation of their results, and their future plans. However, the *ability* to share only translates into actual sharing if there is a motivation to do so. In this chapter we will provide examples of what is possible when researchers choose to share their experimental work in progress. The chapter presents a chronological timeline of some key events in the history of these examples.

25.2 OPEN NOTEBOOK SCIENCE

The term *open notebook science* (ONS) was introduced in 2006 to enable an unambiguous discussion of open collaboration in science [1, 2]. The term *open science* is too broad and nebulous while *open-source science* has been used inconsistently, sometimes referring to open-source software in science. ONS specifically refers to the public sharing of the entirety of one's laboratory notebook, including all associated raw data files. The default assumption is that all experiments from a project are shared in near real time. This allows others to contribute quickly since it can be assumed that, if an experiment is not reported, it has not yet been done [3]. Forms of partial ONS, where there is either a significant delay or selective sharing, can be made explicit by the use of logos [4].

There are some interesting consequences to ONS with respect to collaboration. Since the entire content is shared, not only do others know what has been done in a lab, they can also infer what has not yet been attempted. Potential collaborators can then confidently carry out needed experiments without worrying that they are unnecessarily duplicating work. If they choose to replicate an experiment, then they can do so with the prior knowledge of what happened in all previous attempts.

25.3 USEFULCHEM PROJECT

25.3.1 Platforms

The UsefulChem project was initiated in the Bradley laboratory at Drexel University in the summer of 2005. The concept was to discover and work on urgent problems in chemistry and report on the progress of the project in a transparent way. The project started with the UsefulChem blog on the free and hosted Blogger service provided by Google [5]. A wiki [6] was later established to organize collective information by linking to relevant blog posts or other resources. Wikispaces was chosen as the platform for this purpose because it provided a free hosted service for public wikis and afforded an intuitive visual editor, simplified wikitext, and convenient back-up and alerting capabilities [7].

This model of providing specialized services for free as long as data remain open has been widely exploited for diverse applications on the Web. For example, on Wikispaces, only private accounts require payment. This is a mutually beneficial situation for the client who enjoys free services and for the service provider, where the public accounts provide free examples and testimonials which can serve as a form of advertising for the pay services. Many of these services also monetize the free versions by displaying ads. The first laboratory experiments were recorded on a new blog—UsefulChem Experiments [8, 9]—and information about relevant molecules was collected in posts on the UsefulChem-Molecules blog [10, 11]. The first comment on the Experiments blog from a researcher outside the existing group came from a researcher at the University of Sydney [12], Mat Todd, and provided valuable insight. This contribution was reciprocated later by promoting the Todd group's open project on the chemical praziquantel [13]. Other scientists would continue to periodically comment on later blog posts [14].

By June 2006 it became clear that a blog was not providing the necessary functions for a laboratory notebook, mainly because version control was not available [15, 16]. The plan at this time was to record the laboratory notebook information on the wiki, then copy it over to the Experiments blog when the experiment was finalized. However, in practice, the concept of a "finalized experiment" proved difficult to judge and the wiki was simply used as the actual laboratory notebook. This way errors discovered at any time could be corrected on the wiki with proper version tracking to determine who contributed what and when. The use of a wiki for a laboratory notebook also made it very convenient for mentors to communicate with students by commenting directly on specific sections of a page. The availability of e-mail alerts for any changes on the wiki facilitated very rapid communication.

With the accumulation of data, more effort was invested into providing tools for searching. It was deemed important that both the blogs and wikis be quickly indexed on major search engines. Google Co-op Search allowed for a very simple way of performing a federated search of all of the UsefulChem platforms [17] and was also used later for other multiple ONS resources [18]. Google applications would prove to be key for other sophisticated search and retrieval tools that would evolve over time.

In March 2007 UsefulChem compounds were hosted as part of the eMolecules collection, thereby permitting additional sophisticated services such as substructure searching [19]. The use of Google spreadsheets in UsefulChem for data storage and manipulation proved to be another powerful example of leveraging free hosted resources. Free Google and Sitemeter services also facilitated the discovery of UsefulChem content via license filtering and visitor tracking, respectively [20]. In August 2007 Collaborative Drug Discovery (CDD) provided UsefulChem with a free account to store and share assay results [21]. Neylon's laboratory used another free hosted database application, Dabble, to list people involved in ONS [22].

At the end of March 2007, ChemSpider was first used to manage UsefulChem molecules [23]. A full transition to ChemSpider was completed in June 2007 with the demonstration of substructure searching and the use of the UsefulChem-Molecules blog was discontinued [24]. This free and hosted online chemical database would prove to be integral to many projects. The ability to provide experimental and predicted properties was one of the first essential functionalities exploited. UsefulChem acquired a subdomain on ChemSpider in April 2008 and students were encouraged to upload nuclear magnetic resonance (NMR) spectra of reagents and purified products as open data [25].

In July 2007 a mailing list was created to work through details of challenges related to the UsefulChem project [26]. This was done to capture discussions taking place by e-mail. Collaborators outside of the core UsefulChem team seemed to prefer e-mail over the wiki or blog to communicate and this was done to keep the discussions public.

In April 2008 FriendFeed was first investigated as a collaboration platform for UsefulChem [27]. Its basic function is to aggregate all relevant feeds from various social networking sites for a user to a single account. For example, feeds for all blogs, SlideShare, LinkedIn, Google Reader, YouTube, SciVee, and so on, can be aggregated to one uniform resource locator (URL) [28]. Whenever the user generates a new entry in any of the source accounts, a FriendFeed post is automatically made and reported to all subscribers. Discussions can then take place on FriendFeed itself instead of on the original blog or other type of post. This is particularly convenient since extended discussions on FriendFeed around a post can be referenced with a short URL. Since the open-science community is well represented on FriendFeed, much of the discussion and activity related to UsefulChem now takes place on this platform. This was later detailed in an article in *Chemical and Engineering News* [29].

25.3.2 Medicinal Chemistry: Collaborations Between Synthetic Chemists, Computational Chemists, and Biochemists

The UsefulChem project started with searches on Google Scholar and Scirus in the chemistry category for phrases like "there is a pressing need for," "what is needed now," and "needs to be synthesized." A need for new antimalarial compounds proved to be a recurrent theme [30, 31]. An example of early collaboration spontaneously arose, with renowned blogger David Bradley suggesting to vary the spelling of "synthesize" to the British version of "synthesise" [30].

A deeper collaboration followed the identification of Find-A-Drug as a source of virtual libraries for HIV protease inhibitors [32] and malarial enoyl reductase inhibitors [33]. Find-A-Drug provided a virtual library of diketopiperazines and three-dimensional (3D) docking information of a sample member onto malarial enoyl reductase [34].

The Drexel group started to perform docking calculations using the THINK software [35]. With the intention of adhering to the concept of ONS, the docking runs were recorded using a similar format to wet laboratory experiments so that other researchers would be able to reproduce the computational results and conclusions based on the information provided in the notebook.

A response to an open request for docking collaborators changed the course of the UsefulChem project [36]. A member of the bioinformatics group at Nanyang Polytechnic in Singapore attempted to dock the Ugi product precursors to the diketopiperazine targets and determined that some of them docked onto enoyl reductase. As a result, the problematic cyclization step (see synthesis section below) was abandoned and all subsequent libraries focused on the Ugi products themselves. This is advantageous from a synthetic standpoint since these can be prepared in only one step from readily available starting materials.

In April 2007 Zaharevitz from the National Cancer Institute (NCI) discovered the UsefulChem project through the network of open scientists and offered free testing of compounds for antitumor activity [37]. The first Ugi product was submitted shortly thereafter [38], and in May 2007 the compound was submitted to a tumor inhibition prediction service. Although predicted to be inactive (as was later confirmed [39]), it demonstrated for the first time the "closing of the open-science loop" for drug discovery—where hypothesis formation, docking, synthesis, and assay results were performed openly in real time [40]. This strategy was extended by prioritizing synthetic targets from a virtual library of Ugi products based on the predicted ability to inhibit tumor cell lines. Naphthyl fragments showed up disproportionately in the products with high predicted activity [41]. Zaharevitz further assisted by inviting one of us (JCB) to a National Institutes of Health (NIH) workshop on drug development in January 2008 [42]. Synthetic focus was directed to Ugi product libraries and Guha initiated a malarial enoyl reductase docking study on a 500,000-compound virtual library based on starting materials that could be obtained cheaply and quickly [43]. The most highly ranked compounds from this study were prioritized for synthesis via the Ugi reaction.

Assay results were hosted on CDD and catalyzed the initiation of a new collaboration with the Rosenthal group at the University of California—San Francisco (UCSF), which agreed to run malaria assays for UsefulChem compounds at no charge. The Rosenthal group had previously discovered the malarial enzyme falcipain-2, and it was convenient for them to run an inhibitory assay against that protein, in addition to red blood cell assays to measure the inhibition of infection by the malarial parasite [44]. The focus of the work thus shifted from enoyl reductase to falcipain-2. With a crystal structure and known binding site, docking calculations were performed and two Ugi products in the top 1000 from Guha's docking results were synthesized and shipped to the Rosenthal lab in December 2007 [45]. Activity at the micromolar range against both the enzyme and the infection of red blood cells by the parasite was reported in January 2008 [46]. By August 2008, 4 of the 17 Ugi products tested showed similar results for inhibition of the enzyme and infection [47], clearly a very impressive proof of principle.

25.3.3 Chemical Synthesis Strategy: Collaborations Between Synthetic Chemists, Both Locally and Remotely

A general synthesis was proposed to generate the putative malaria inhibitors suggested by Find-A-Drug, which were based on a 2,5-diketopiperazine scaffold [48]. Further literature searching revealed some examples of the diketopiperazine synthesis on solid support [49, 50]. Finally, in December 2005, a more convenient solution was found based on a Ugi reaction followed by a cyclization [51].

One of the required starting materials for an Ugi-related synthesis strategy to many of the members of the diketopiperazine library was the compound known as DOPAL (3,4-dihydroxyphenylacetaldehyde). This compound could not be purchased and the synthesis of DOPAL therefore became a primary synthetic focus. A question arose as to whether the presence of a phenolic group would interfere in the Ugi reaction [52]. This concern was greatly diminished by a contribution from ChemRefer, where an article reported that an electron-withdrawing group on the aromatic ring is necessary for the phenol to participate in the Ugi reaction [53]. Feedback from an expert in the field supported this assessment [54].

Synthetic methods to prepare DOPAL were discussed on the blog [55] and the synthesis was finally solved in October 2006 [56]. Progress was slowed by errors in the literature. However, a report [57] detailing these errors and linking to the "failed experiments" that uncovered their discovery demonstrated that ONS could be useful for providing more transparency in science and saving time in the future for anyone attempting to repeat the synthesis.

Unfortunately, DOPAL and similar aldehydes proved to be too susceptible to side reactions, and other more stable compounds were used to try to understand the behavior and kinetics of the Ugi reaction first [58, 59]. Research work often has to deviate from initial plans due to unexpected problems. However, the nature of those problems is not usually communicated in sufficient detail (or at all) via traditional channels. In a sense, making the details of these problems easily indexed on major search engines is a type of collaboration with future researchers who may run into similar problems and benefit from the details provided.

25.3.4 Cheminformatics: Collaborations Between Chemists and Programmers

The representation, manipulation, and communication of chemical information in an open-science environment is not a trivial challenge. One of the earliest cheminformatics tasks consisted of converting the format of the first malaria virtual library to one that was easier to share publicly. One of the Find-A-Drug volunteers contributed by providing the library as a simplified molecular input line entry specification (SMILES) list [60], a text-based format consisting of a string of characters that can be easily manipulated in spreadsheets [61]. The discovery of open-source software such as Open Babel [62] would also prove to be critical for the cheminformatics needs of the project. An ecosystem of open science related to cheminformatics evolved over time. Projects with overlapping objectives naturally interlinked at a convenient level. For example, the UsefulChem project had a presence on The Synaptic Leap for the purpose of finding collaborators [63], including a suggestion for a free docking program [64]. Several key individuals with overlapping interests started blogging about their cheminformatics work. Willighagen started CML Explained [65], Apodaca blogged on Depth First [66], Murray-Rust started the CML blog [67] and PeterMR's blog [68], and Williams maintained the ChemSpider blog [69]. Simply following each other's blogs turned out to be a fairly efficient way for the community to collaborate on shared interests. An excellent example of this took place in September 2006 when Willighagen suggested that the Open Source JSpecView applet could be used to view NMR spectra in JCAMP-DX format [70], and this became immensely important to sharing and manipulating raw data from UsefulChem [71], including the monitoring of reactions [72]. The ability to use JSpecView to overlay NMR spectra was particularly useful for monitoring reactions [73] and measuring kinetics when integrated with Excel VBA [74, 75].

Chemical Markup Language (CML) represented a promising way of openly sharing chemical information. As we attempted to create CML really simple syndication (RSS) feeds from our molecules blog, Willighagen and Murray-Rust shared their expertise [76]. It may be better to characterize this type of interaction as a metacollaboration since it did not involve project-specific objectives so much as general ways of representing and manipulating chemical information publicly. Lessons learned in this space would prove to be valuable for quickly starting other chemistry open notebook projects, including the conversion of laboratory notebook pages describing a Ugi synthesis into CML [77].

Willighagen proposed a method of introducing tags into blog posts to make the molecules discussed machine readable [78]. This was experimented with for the UsefulChem blog and provided a new means for potential collaborators to find information via the Chemical Blogspace, an aggregation service for chemistry blogs. Further collaborations ensued. In June 2007 Guha created a public Web service to generate a combinatorial list of all Ugi products resulting from lists of starting materials represented as SMILES [79]. Shattuck created a Web service to deconvolute NMR spectra using JCAMP-DX files as input [80], and in August 2007 an account was created on MyExperiment to attempt to process and organize Web services related to the UsefulChem project [81]. However, productive use of this system would have to await the involvement of new collaborators after the creation of the ChemTaverna project in 2010 [82].

In November 2007 enough data were being generated in the laboratory notebook that it made sense to start abstracting Ugi reaction information into a Google Spreadsheet to compile a CombiUgi Master Table [83]. Since each record points to the corresponding laboratory notebook page, information is not lost, but the abstraction allows for semantic querying of the data set. Attempts were also made to convert the workflows into organized machine-readable formats, involving a discussion between others (Williams, Willighagen, and Murray-Rust) interested in overlapping objectives [84, 85]. In April 2008, Guha created the first version of a model to predict precipitation from methanol based on molecular descriptors of the products [86].

In March 2010 the reactions recorded in the UsefulChem notebook were abstracted into a machine-readable format as part of the Reaction Attempts (RA) database [87]. In April 2010 the first edition of the RA book was published in conjunction with the first archive of the UsefulChem laboratory notebook and associated raw data files [88]. The RA database also started to abstract reactions from other open notebooks, like the one shared by the Todd group on the Synaptic Leap [89]. The usefulness of sharing the abstracted information from open notebooks became clear in June 2010 when attempted reactions revealed an overlap between the Bradley and Todd groups, allowing for a very efficient collaboration and sharing of details about challenges beneficial to both groups and anyone else with an interest [90]. A Web-based Reaction Attempts explorer was also created to allow searching by reactant or product drop-down menus or substructure [91].

25.3.5 Second Life

Long-lasting collaborations can spring from some unusual places. While exploring the virtual world Second Life as another channel to communicate open notebook information, a contact was made between two of the authors, Bradley (JCB) and Lang (AL) [92]. The first collaborative project involved improving the 3D Second Life molecule rezzer developed by AL so that it could be used easily by simply supplying a SMILES in the chat box to generate the molecules with a realistic 3D conformation [93]. This permitted a display of Ugi products, enoyl reductase, and slides from a recent presentation, all hyperlinked to either blog posts or laboratory notebook pages for further details [94]. An effort was then made to index molecules in Second Life on a wiki [95].

In June 2007 a collaboration between an extended team resulted in a 3D animation demo of the docking of a Ugi product into the binding pocket of enoyl reductase via four hydrogen bond sites [96]. An interactive 3D animation of the formation of imine—the first step in the mechanism of the Ugi reaction—was displayed in Second Life in August 2007 [97]. These are powerful demonstrations of how sophisticated representations of research within an open notebook can be leveraged from the contribution of expertise from several individuals brought together for rapidly implemented applications.

25.3.6 Requesting Collaboration

In March 2006, JCB requested help with disabled instrumentation on the UsefulChem blog [98]. It is interesting to note that most specific open requests of this type were not directly answered. Most of the collaborations to arise from the project did so based on a shared overlap of interests, and this often caused a shift in project direction. Flexibility is of paramount importance when embarking upon these types of collaboration—all parties need to benefit. This experience suggests that open-science platforms primarily based on very specific tasks and questions may find it difficult to thrive. For example, the discussion forum ChemUnPub did answer one of our questions but did not result in a long-term collaboration [99]. A question on the OrgList mailing list was also helpful for a specific laboratory cleaning procedure [100].

25.3.7 Sharing Drafts of Papers and Proposals

In April 2007 drafts for a paper [101], a thesis [101], and a proposal [102] related to UsefulChem were started on the wiki. Being quickly indexed on major search engines, these documents represent a new way to share research work as it is being organized and planned. This is especially the case for proposals, which are rarely made public at any point. Nature Precedings, which provides a platform with an easily citable format including an author list and DOI [103], was used to publish another proposal for the project in January 2008 [104]. In June 2008, Nature Precedings no longer accepted proposals and so a proposal to the Gates Foundation was made public on Harel's S.C.I.E.n.C.E wiki, set up for this purpose [105], and Scridb [106].

As for drafts of papers, not all instances of started drafts end up as submissions to journals in a rapid and straightforward way. If the drafts are always public and indexed in search engines, there is a chance for someone to make use of even partial information from the very start. For existing or potential collaborators, this information can facilitate a deeper understanding and more efficient exchange of ideas, especially when the proposals or drafts of papers reference experiments in open notebooks. Writing a paper on a wiki essentially is a form of preprint, and journal guidelines should be consulted for subsequent submission for peer-reviewed publication [107]. Reports about other students writing up at least a part of their thesis openly started to appear [108].

25.3.8 Media Coverage: Collaborations with Journalists and Authors

By definition, a collaboration involves any situation where two or more parties work together to the benefit of all involved. In the case of ONS, journalists and authors of review articles in both the popular media and the peer-reviewed literature turned out to be important collaborators. The journalists obtained material for their pieces on the changing dynamics of scientific collaboration and the open-science movement and projects like UsefulChem received a significant amount of coverage that often led to new collaborations with other scientists as a result. News coverage also proved to be critical to lending legitimacy to the effort allowing the Wikipedia entry on ONS to be accepted in October 2008 [109, 110].

25.3.9 Other Open Notebook Science Projects

The foundation work established in Bradley's work has catalyzed a number of other ONS projects, including a platform to share research proposal ideas in natural product synthesis which became the wiki TotallyRetrosynthetic [111], a laboratory notebook for Faith [112], and a blog and wiki for the Rosania team based on the UsefulChem template to track his work on subcellular drug transport [113, 114]. The Rosania group also extended the reach of sharing their experimental results on Second Life [115].

25.3.10 Other Types of Collaboration

The UsefulChem project experimented with another form of collaboration: guest blogging. David Bradley reported on open access in chemistry [116, 117] and arsenic remediation projects [118]. On occasion a student would submit a post, but over time the UsefulChem blog evolved to a single-author modality. An unexpected collaboration arose involving the interaction of students in the humanities with the UsefulChem project [119]. The UsefulChem Writing Partners program required students from the Ritter–Guth group at Lehigh Carbon Community College to write less technically about UsefulChem themes, especially malaria [120]. This was beneficial for both the humanities students to understand how science is done and for the chemistry students to try to explain their research to a wider community.

In July 2006 an anonymous commenter brought up the issue regarding whether patents can help or hinder humanitarian applications [121]. This is an example of a type of collaboration originating from working openly, where larger issues and concerns can be addressed early on. We also found that "accidental collaboration" was occasionally very useful. For example, by monitoring search terms on Sitemeter, we discovered that water was a viable and potentially better solvent for Ugi reactions [122].

In November 2006 an offer was made to provide compounds on a "copyleft" basis, the concept being that samples of products made in the lab that could be spared would be provided freely—as long as the research done with those compounds was made open immediately [123]. Thus far no requests for this type of collaboration have been made.

In May 2008 another opportunity to collaborate with a company arose. Mettler-Toledo lent Drexel a liquid-handling robot to carry out Ugi reactions using more automation [124, 125]. An optimization study was done and the problems encountered with the use of such a parallel strategy were reported [126]. In addition, the *Journal of Visualized Experiments* (JoVE) contributed by sending a cameraman to record a video to document the execution of the reaction [127]. The JoVE article, composed of a conventional text portion and a video, was published in November 2008 [107].

A first attempt was made to allow collaboration via a specific page for anyone to request experiments to perform [128]. No requests were made from this attempt, although this strategy was successful for requests of solubility measurements. For example, a request for the solubility of pyrene in acetonitrile was made from a group in Israel to assess soil contamination, and the Drexel group provided an answer within days. A Google spreadsheet was set up to collect all such solubility requests from either people or autonomous agents [129]. Early on, related projects were discovered. These include the e-malaria project at Southampton University [130] and the Synaptic Leap [131]. A connection with Southampton University and the Synaptic Leap would eventually intersect with UsefulChem in important ways. A collaboration between JCB and Mesa Analytics and Computing via a Small Business Innovation Research (SBIR) award demonstrated that it is possible for academia and industry to work openly on a drug discovery software project [132]. X-ray crystallographer Matthias Zeller from Youngstown State University contributed to the UsefulChem project by providing a crystal structure for one of the Ugi products [133]. In June 2008 Richard Stephenson from Southampton University further contributed by setting up an eCrystals repository for Drexel where UsefulChem crystal structures could be shared openly [134]. A collaboration with Brent Friesen at Dominican University was initiated involving the synthesis of new Ugi products in his sophomore organic chemistry teaching laboratory [135, 136]. He incorporated the ONS Solubility Challenge as the first week of his laboratory [137]. The Spectral Game was made available on Second Life [138] and then on the Web [139]. It was reported a few months later in a paper in the *Journal of Cheminformatics* [140]. This was only possible because of the contributions of NMR spectra by chemists as open data when uploading to ChemSpider. This includes spectra that are routinely obtained as part of the UsefulChem project and demonstrates that, by making data open, collaborative projects not initially imagined at the time of submission can quickly arise.

The usefulness of reporting raw laboratory notebook data was demonstrated in the summer of 2009 when an article with surprising results appeared in the *Journal of the American Chemical Society* [141], specifically the observation of an oxidation by a reducing agent. Social networks such as FriendFeed spread the information very quickly and to enough chemists that two groups (UsefulChem and Totally Synthetic) attempted to reproduce some of the experiments and another found a precedent from the literature explaining the phenomenon. In this case it was critical for the two groups to produce the raw NMR data which could be unambiguously interpreted by the chemistry community. Simply reporting without proof that the experiment had not worked would not have been unequivocal.

25.4 OPEN NOTEBOOK SCIENCE SOLUBILITY CHALLENGE COLLABORATIONS

25.4.1 Crowdsourcing Solubility Measurements

In September 2008 the ONS Challenge was announced to attempt to crowdsource the measurement of nonaqueous solubility using open notebooks based on the same Wikispaces and Google spreadsheet platforms as the UsefulChem project [142]. There are currently about 200 specific solubility queries per day utilizing the results of the Challenge, originating mainly from Google and

Wikipedia [143]. The query results ultimately lead to the relevant lab notebook pages and raw data for anyone who wants to track the ultimate provenance of the data [144].

25.4.2 Sponsorship

Sigma-Aldrich sponsored the Challenge by contributing chemicals on an as-needed basis [145]. The first shipment was sent in February 2009 [146]. In October 2008 Submeta sponsored the ONS Challenge with ten $500 prizes to be awarded approximately once a month to students in the United States and the United Kingdom [147]. In November 2008 Nature committed one year subscriptions to the *Nature* journal for the first three winners of the ONS Challenge [148]. The first winner was announced at the end of November 2008 [149]. The Royal Society of Chemistry sponsored another five prizes in March 2010 [150].

25.4.3 Gaining Experience by Laboratory Rotations

In June 2009 the collaboration evolved to include face-to-face interaction when a student, David Bulger (February 2009 Submeta Award winner), spent a few weeks at Drexel with JCB, then with Cameron Neylon (CN) at Southampton University, to learn laboratory techniques before returning to Oral Roberts University with AL [151]. The stay at Drexel helped resolve some issues about the reliability of using NMR to measure solubility [152].

25.4.4 Solubility Modeling and Visualization

Several programmers collaborated with chemists to provide interfaces to the solubility data set as well as build models. This included a way to intuitively navigate the data over a Web browser [153, 154] or Second Life [155] and allow substructure searching [156]. The data set was also converted to resource description framework (RDF) to extend its use to a broader group [157]. A solubility model based on Abraham descriptors was made freely available [158]. Ultimately, both the UsefulChem Reaction Attempts and the ONS Solubility Challenge databases were combined to generate a Solvent Selection service that could be used in principle for any reaction where high solubility of reactants and low solubility of the product are desired [159].

25.4.5 ChemTaverna and MyExperiment

Recently, it was demonstrated that the solubility and reaction Web services created for the UsefulChem and ONS Solubility Challenge can be integrated into ChemTaverna and shared on MyExperiment [82]. By putting these tools into the hands of a vibrant community already using this platform for bioinformatics, it is hoped that future collaborations in the area of cheminformatics will be greatly facilitated.

25.5 OPEN NOTEBOOK SCIENCE IN UNDERGRADUATE PHYSICS LABORATORY HOSTED ON OPENWETWARE

25.5.1 Overview

For the four fall semesters of 2007–2010, ONS has been carried out by physics students enrolled in a junior laboratory course at the University of New Mexico (2007 [160], 2008 [161], 2009 [162], 2010 [163]). The experiences have been summarized in blog posts [164, 165]. The fully public electronic notebooks are hosted by OpenWetWare (OWW), a service initiated in 2005 by students in the Endy and Knight laboratories at the Massachusetts Institute of Technology (MIT) [166]. OWW currently has over 8000 members and its primary funding is through a grant from the National Science Foundation [167]. All student work is recorded and presented on the public wiki, and almost all instructor feedback is presented on the same wiki pages [168]. The only nonpublic information is the letter grade for the work. From 2007 to 2010, approximately 60 students have participated in the ONS course, with most of them majoring in physics, astronomy, math, or a combination of those. No effort was made to formally track the students, but the instructor knows that at least six students from the 2007 and 2008 semesters have since enrolled in Ph.D. programs. Two students from those semesters have begun teaching high school physics. Many of the students continued to use OWW after completing the junior laboratory course for a variety of purposes, including other lab courses [169] and undergraduate research [170].

25.5.2 Description of How Students and Instructor Carry Out ONS

There are three types of work that junior lab students record in their public pages on OWW: a primary laboratory notebook [168], informal laboratory summaries [171], and one formal research report [172]. For the purposes of this report, we will focus on the primary laboratory notebook in the context of one laboratory "cycle." The students complete six individual laboratories throughout the semester, and they are free to work alone or in groups of two. We will describe typical workflow for one of these cycles.

25.5.2.1 Preparation and Safety After choosing a laboratory to work on for the subsequent two three-hour lab sessions (three hours in week 1, three hours in week 2), students are required to do background reading so that they have a good understanding of what their goals will be, what kind of equipment they will need, and especially what the safety hazards will be. When they feel they are fully prepared, they will ask the instructor or the teaching assistant to carry out their "safety quiz." The instructor or TA asks the students to explain the work and to identify the main personal safety hazards and then potential hazards to the equipment. This exam is carried out orally. Many students will record safety issues in their primary laboratory notebook, with by far the most common safety hazard being electrical shock [173].

25.5.2.2 Primary Work (Equipment Setup, Data Acquisition, Data Analysis) Each student has a designated area on the wiki for recording electronic notes detailing his or her work while setting up an experiment, taking data, and analyzing data. Students have leeway as to how they organize their work, but the default method is a chronological system based on OWW's lab notebook with one-click setup [174]. Primary notebooks of students from prior weeks or semesters have become the de facto laboratory manual for the course. When performing background research for the laboratory work, the instructor has observed that most students refer to other students' lab notebooks in combination with a lab manual from the prior instructor [175]. This behavior is encouraged, as is citing and linking to those resources.

The instructor has observed that students' primary notebooks have converged on a structure that is a mix of chronological and topical recording of notes. A general structure that has emerged is for the primary notebook to have the following sections: title, purpose/overview, equipment and setup, data, data analysis and code, results/link to results summary, discussion of errors, and acknowledgments. This is not a rule and students are free to record their information in a variety of formats provided sufficient information is recorded. A guiding principle that the instructor dictates is that the main purpose of the electronic laboratory notebook is "reproducibility." For the purpose of the junior laboratory, "reproducibility" is defined as the ability for the same student to replicate the experiment one year later using only his or her own laboratory notebook as a guide. Students should imagine whether they would be able to obtain measurements with similar amounts of random and systematic errors after their memory has faded over the course of a year. Anecdotally, this appears to be an understandable goal for the students.

25.5.2.3 Equipment Setup Students are required to record the make and model number for all the equipment used during their experiments. They are also required to record how the equipment are set up and detailed procedures for obtaining data. From 2007 to 2010, there has been a marked increase in the percentage of students who have smart phones in the laboratory. This has correlated with an increase in the usage of digital photographs to describe the setup of the experiment. This behavior is strongly encouraged by the instructor.

25.5.2.4 Data Acquisition Students are required to record their data electronically and to display the data and detailed notes about how the data were acquired in their public notebooks. A common problem with any electronic notebook is difficulty in capturing information and data without disrupting the experimenters' ability to work. In particular, for the junior laboratory, it takes some effort to record data in the wiki, especially tabular data. Uploading images also requires many manual steps. Finally, light from computer screens is sometimes too bright for use next to an experiment with a dim signal (such as during optical spectroscopy by eye). OWW is run on a MediaWiki engine, the same engine used for Wikipedia [176]. This allows for many extensions and widgets. Flanagan, lead developer for OWW, has implemented many of these widgets, many of which attempt to make it easier to capture information into a laboratory notebook. One of these allows easy embedding of a Google Docs spreadsheet [177]. Junior laboratory students are encouraged to innovate and try out different ways of using their laboratory notebook. In 2007 students struggled with wiki or Hypertext Markup Language (HTML) tables for recording data. By 2009, the majority of students used Google Docs spreadsheets for recording data. A major advantage of this is easy recording of information that is autosaved and easy to share with the world. A drawback is that the information in the spreadsheets is currently not archived by OWW, so an electronic laboratory notebook is not a self-contained entity.

Many students record data directly into Google Docs, into the wiki, or into another electronic resource, such as Evernote [178]. However, it should be noted that even in 2010, with the ubiquity of smart phones and Web-based resources, a number of students resort to recording notes on paper and then transferring them to electronic form later. One simple reason for this is that some laboratories require dark-adjusted eyes which are not achievable when using even a smartphone. Another reason is that some students continue to find pencil and paper the fastest, easiest, and/or most comfortable means of recording information. These are the anecdotal observations of the instructor, and in his opinion it remains a problem with ONS or electronic lab notebooks more generally. The instructor does not require students to discontinue use of paper, provided they subsequently copy their notes to the primary electronic notebook.

25.5.2.5 Data Analysis Students are required to record their data analysis procedures and results in their primary laboratory notebook. It is stressed that this information is an important component for reproducibility, including the type of software used, spreadsheets, and code. For example, students will embed or link to their spreadsheets (typically Microsoft Excel or Google Doc) or they will upload their original Matlab code [179]. Important functions used for processing the data (such as LINEST) are highlighted.

25.5.2.6 Informal Lab Summary For most laboratories, in lieu of a formal laboratory report in the style that would be submitted to a typical peer-reviewed journal, students instead produce short, informal laboratory summaries that are separate from their primary laboratory notebook [171]. As described below, the students produce one formal report that includes a rough draft with extensive instructor feedback. The informal summaries are on separate wiki pages from the primary laboratory notebook. In the summaries, the students give a brief overview of the laboratory, report their final results, and discuss any discrepancies with accepted values, sources of systematic and random error, and ideas for improving future measurements. They link to their primary laboratory notebooks as the underlying resource for any readers wanting to reproduce the work or understand it better. On either the informal laboratory summary page or the primary laboratory notebook, students are required to acknowledge and link to helpful resources they relied on to carry out the work, such as other students, the laboratory manual, Wikipedia, and so on, to helpful resources, either on a summary page or primary laboratory notebook.

25.5.2.7 Instructor Feedback When students have completed their laboratory summary, they "hand in" their work by sending the instructor an e-mail with a link to the summary. The instructor puts comments, compliments, and criticism "in the margins" of the work by directly editing the wiki. For the one formal report, instructor feedback on the rough draft is extensive, attempting to explicitly point out all deficiencies that need to be worked on. Thus, almost all of the student work and instructor feedback is publicly visible to the world, with only the letter grade and perhaps other e-mail communication kept private. As the semester progresses, the volume of instructor feedback diminishes greatly, and usually feedback for the final informal summaries is not given. The instructor's impression is that feedback earlier in the semester is more valuable. Furthermore, student work seems to improve greatly after feedback is given for the first summary.

25.5.2.8 Formal Report For one of the laboratories of their choosing, the students are required to prepare a formal report in the style of a typical peer-reviewed publication. A rough draft of this report is due in approximately week 12 of the 16-week semester. This report is "handed in" to the instructor by e-mailing a link to the wiki page. All feedback by the instructor is put in "the margins" as with the other feedback. This feedback tends to be more extensive than with informal summaries [172]. A letter grade for the rough draft is e-mailed to the students privately. This letter grade is typically a D or C to indicate the amount of improvements needed, but students receive full credit as long as they hand in the rough draft on time and with sufficient effort having been made. During the final week of the semester, the students work in the lab to repeat the experiment for which they're writing their formal report. The goal is to implement some of their ideas for improving their measurements after having thought deeply about the work while writing the formal report. The final draft of the formal report is due at the end of the semester [180].

25.5.3 Outcomes (Anecdotal)

An effort has not been made to scientifically track the impact of ONS in this laboratory course. In order to do so, measurable goals would need to be defined and students would need to be tested before and after the course. Instead, the instructor has so far relied on anecdotal observations. He has observed many positives from the use of ONS. Students routinely read each others' laboratory notebooks and give credit for the assistance. Building upon prior work and citing it properly are fundamental aspects of science, and it appears that ONS strongly promotes learning this skill. It appears that the quality of measurements and sophistication of data analysis methods have improved every year. One experiment to follow through the years is the Millikan Oil Drop experiment, where students attempt to measure the value of the electron's charge, *e*. An example from 2007 is found from Le's primary notebook entries [181, 182]; another from 2008 is provided by Osinski [183, 184] and one from 2009 is provided by Callow [185–188]. Interestingly, Callow's work drew some interest from other scientists on a FriendFeed thread [189].

This would be an expected outcome of students building upon prior students' work. Another positive aspect of ONS in this course is that students can implement ONS in their future research careers. Some students have already done so [190]. It is hypothesized that a positive ONS experience in this undergraduate laboratory course will increase the likelihood of carrying out ONS in the future, especially after having become a principal investigator who can dictate laboratory notebook policies. Finally, another positive result has been the transfer of ONS techniques from the teaching laboratory to the instructor's research laboratory, for example, use of embedded Google Docs and other techniques to increase the ease of capturing information in the lab. The positives appear to have far outweighed the negatives, which are difficult to find. One negative could be that ONS has reduced the effort students need to exert to get an experiment to work. So, it is plausible that they are developing less hands-on skills than students who start "from scratch." Another possible negative is that students can balk at presenting their work publicly, and their creativity and performance could suffer significantly. While plausible, the instructor has not yet detected this outcome. Overall, feedback from students has been overwhelmingly positive—this comes from direct communication as well as from anonymous end-of-semester course evaluations.

25.5.4 Future Work and How to Replicate

What is needed for other instructors to carry out ONS in their own courses? As long as an electronic platform for ONS is available in the laboratories, extensive planning is not required. In the case study described here, the instructor simply decided that students should do ONS, provided them with accounts on OpenWetWare, and set them loose. While somewhat chaotic at first, the outcome was delightful. If there are resources for planning the course, there are some things that could be carried out better, especially in terms of assessment. As mentioned above, pre- and posttesting of students are essential to know with certainty that ONS is impacting desired outcomes. Similarly, mechanisms should be developed to keep track of alumni of these courses in order to assess whether ONS in the undergraduate teaching lab affected their future research behaviors or opinions toward ONS or other open-science ideas.

25.6 LABORATORY BLOGGING: FRAMEWORK FOR SMALL-SCALE COLLABORATION

The laboratory notebook system developed at the University of Southampton in Frey's group [191] has formed the basis for the primary laboratory record for one of us (CN) for nearly five years [192]. Over time this has been used in a range of different ways and with different organization schemes [193], but here we will focus on its role in supporting collaborations, particularly geographically distributed ones. The system is similar to most blog engines in being organized into posts, usually presented in reverse chronological order, an ability to comment, including people other than the post author, and the generation of RSS feeds of posts. These main features, which are relevant to the discussion of collaboration per se, are common to almost all blog engines. Most of the other technical capacities of the system are not relevant to this discussion, but one difference is important. Posts within the Lab Blog system cannot be deleted by the user, consistent with best practice in retaining a permanent record of the research process. Where changes are made to a post, a full version history is maintained, effectively enabling a final version of the record to be presented by default but providing the complete detail of changes or mistakes to be available if required.

25.6.1 One-to-One Collaborations

The most successful collaborative projects that have been supported by the blog system have been largely one-to-one interactions. In the first, the supervision of a student based at Southampton by CN was effectively supported by the system after he had moved to a new site [194, 195]. The system enabled a close interaction on a daily basis with the details of the experimental work. The details of experimental protocols and results could be discussed in close to real time despite the geographical distance. From a technical perspective this was achieved through the monitoring of the RSS feed for the student's blog in Google Reader. This functioned mainly as a notification system as Google Reader did not display many elements of the rendered post correctly, due to the loss of formatting information in the XML of the RSS feed. Commenting and communication would occur back on the blog system rather than through any third-party service. This pattern has been more or less repeated in subsequent collaborations, both those taking a completely open approach and exposing the record freely on the web and cases where the interaction has been through a closed, password-protected blog.

25.6.2 Failures

There have also been a number of attempts to utilize the system to support collaborations that have failed. On the surface these have many characteristics of the successful examples: geographical dispersion, an acceptance of the value of Web-based record keeping, and a desire to maintain a high-quality record. In some cases these efforts have even involved groups on the same site. However, a common feature of all the failures is that the use of the blog was for only a portion of the work being undertaken. In some cases this was due to multiple projects being run, only one of which was being recorded in this manner. In other cases problems arose due to the confidentiality of portions of a project that could be entrusted to the level of security available within the system.

The clear end result is that where the record becomes split the nontraditional record, usually the one that for either technical or social reasons requires more effort to keep up to date, suffers and falls behind. Once the record keeping falls behind or is temporarily recorded in some other form, it rarely catches up again. This is not by any means a specific characteristic of the blog-based notebook and is likely to be true of the use of any new system. However, the lack of geographical colocation and consequent lack of "nagging" available to encourage use as well as the limitations of the user interface for the blog system exacerbated these issues. The lack of peer pressure that resulted from primarily one-to-one as opposed to wider group collaborations was also a contributing factor.

25.6.3 Scaling the Collaboration

It appears that a blog-based system, where posts and comments are clearly attributed to one author, provides a somewhat more personal space that is more suited to one-to-one collaborations. The splitting of each person's record into individual blogs also seems to encourage this, making it less likely that community members will directly contribute to or edit each other's material. In comparison, the Wiki-based systems used in the UsefulChem and ONS Challenge projects provide a single unified space, where direct editing of content is supported and encouraged, but commenting less so. In the wiki systems an approach of commenting in line has been adopted, due largely to the need for comments to be closely associated with the relevant text. The more modular nature of the way the blog system has been used means that separate comments do not drift away from the relevant text as much as is the case with the talk page on the wiki system. These different approaches to commenting, in separate comments in the blog and directly in the text of the wiki, may mean that the wiki provides less of a sense of personal ownership of the text. By comparison the blog system supports a back-and-forth conversation in the comments that may be felt to be more personal. There is a balance to be struck here between the need to give people space to feel comfortable to write and the need to support effective communication. The system as it currently exists requires some form of account to comment or contribute. This has limited direct contact with external users.

Supporting larger-scale collaboration in the context of the blog system will require careful attention to the integration of notification schemes, of both posts and comments. The personal nature of posts may assist in making people more comfortable with describing their work in a public space by avoiding the additional fear of having their text edited. However, at the same time it does not encourage the more direct interaction that appears to be supported by wiki-based systems. A key aspect for both systems is effective notification of the community when new content has been created. There is a significant technical infrastructure available that supports this for blogs, including RSS feed manipulation tools like Yahoo Pipes and collaborative RSS reading environments such as Google Reader where content can be shared, tagged, and commented on. The configuration of this for specific projects will require care. Both blogs and wikis suffer from a problem in notification where important changes are made to a post or page. In the case of most blogs modifications are not posted to the feed, whereas for wikis in general the feed contains all committed changes. Neither of these extremes is helpful, and in addition the useful display of changes to a preexisting document remains a challenge. The effective notification of significant or important changes is an important technical challenge for the effective use of collaborative online tools for recording research.

25.7 CONCLUSION

Collaboration on many levels can be facilitated by ONS and other open-science projects. However, getting things done generally requires a specific person to champion a specific subset of tasks [196]. Fortunately, there have been enough collaborators during the past few years in the open-science community with enough shared goals between projects to enable useful tools and resources to emerge.

Concerning collaborative platforms, for UsefulChem, an evolution took place over the course of the project. Initially blogging and commenting on blogs was a significant means of public communication. A blog was tried initially to host the actual laboratory notebook, but limitations quickly led to migration to a free hosted wiki on Wikispaces and raw numerical data stored in public Google spreadsheets. A mailing list was in use for a brief time to facilitate public communication with collaborators. However, in the latter half of the ONS projects at Drexel and much of the open-science community, FriendFeed became a very important mode of public communication.

In the case of using OpenWetWare for teaching laboratory applications, the flexibility of ONS allows implementation without excessive planning. The ability for students to view each other's work and the ease with which the instructor can provide specific feedback are strong assets to this approach.

The Laboratory Blog system has demonstrated that a blog-style framework is a useful way of generating an online research record. It seems particularly effective at supporting the small scale, particularly one-to-one collaborations and monitoring of student work. The use of one blog per person and a lack of integrated notification frameworks make it more difficult to scale these collaborations using this system. Successful implementation of these systems requires an all-or-nothing approach. Mixed record keeping always favors the incumbent system.

As long as there is an intent to share and be open, the platforms of communication can continue to change—as they have in the past—without the risk that conversations will stop. The trend has been toward tools that make it easier to collaborate and discuss—and the use and combination of multiple platforms to leverage what each does best. This redundancy is beneficial in a world where it is not possible to predict which technologies and services will be dominant or even available a few years down the road.

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