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**Collaborating with Undergraduates to Contribute to Biochemistry
Community Resources**

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Abstract

Course-based undergraduate research experiences (CUREs) have gained traction as effective ways to expand the impact of undergraduate research while fulfilling pedagogical goals. In this Perspective, we present innovative ways to incorporate fundamental benefits and principles of CURE courses into a classroom environment through information/technology-based research projects that lead to student-generated contributions to digital community resources. These “CoRe” projects represent an attractive class of CUREs because they are less resource-intensive than laboratory-based CUREs, and the projects align with the expectations of today’s students to create rapid and publically viewable contributions to society. We provide a detailed discussion of two example types of CoRe projects that can be implemented in courses to impact research and education at the chemistry-biology interface: bioinformatics annotations and development of educational tools. Finally, we present current resources available for faculty interested in incorporating CUREs or CoRe projects into their pedagogical practices. In sharing these stories and resources, we hope to decrease the barrier for widespread adoption of CURE/CoRe approaches and generate discussions about how to utilize the classroom experience to make a positive impact on our students and the future of the field of biochemistry.

The shifting state of biochemistry.

The way we teach biochemistry to undergraduates is undergoing a paradigm shift. Gone are the days in which the biological significance of chemistry is squeezed into the last week of an organic chemistry course. Biochemistry is front and center: it is a foundational subdiscipline as defined by the American Chemical Society, and the biological relevance of chemistry is now a core competency defined by the American Academy of Medical Colleges (AAMC).¹⁻⁵ These changes have sparked innovation in the classroom to emphasize the breadth and relevance of the chemistry-biology interface.⁶ These developments also reflect our new audience: Today’s college students come from the cohort commonly referred to as “Millennials”, a population described as “optimistic”, “confident”, and “always connected”.⁷ Students do not want to wait to know the usefulness and applicability of core concepts, and they arrive at college eager to make meaningful contributions to their communities. They are looking for earlier entry into research, and thus course-based undergraduate research experiences (CUREs) are emerging as a means to engage students while fulfilling the evolving pedagogical goals of biochemistry education.

In this *Perspective*, we discuss an emerging class of CUREs that focus on information/technology-based research projects that lead to digital contributions to

community resources (CoRes). We provide a detailed discussion of two types of CoRe projects that can impact the chemistry-biology interface: bioinformatics and educational tools. Finally, to generate ongoing discussions about these approaches to teaching biochemistry, we present resources available for faculty to share and view documents and details related to biochemistry CUREs and CoRe projects.

Collaborating with undergraduate students through course-based research experiences.

Historically, the ways in which undergraduate students have directly and positively impacted the field of biochemistry is via undergraduate research opportunities in faculty research labs, which can lead to publication.^{8,9} These traditional research internships benefit both students and faculty,^{10,11} but the critical challenge remains that most institutes lack the capacity needed to accommodate every interested undergraduate student in a faculty lab. Incorporating research activities into coursework provides a powerful solution to this challenge along with many other benefits for both faculty and students. As a result, increasing numbers of faculty have been inspired to “throw away the cookbook”¹² and implement CUREs in their lab courses. Table 1 highlights selected examples of CUREs at the interface of biology and chemistry, demonstrating that this pedagogical approach is viable across different institutional contexts and can focus on a range of course themes. The table was generated from responses to a call for CURE examples on the CURE Facebook group page “Adding Research to a Class”. The faculty listed in the table encourage readers to reach out to them for more information about implementing CUREs and/or potential collaborations.

Table 1. Examples of CUREs at the interface of chemistry and biology generated from responses to a call for CURE examples on the CURE Facebook (www.facebook.com) group page “Adding Research to a Class”.

Faculty Member	Course Level	Enrollment	Research Project Description
Kelly Barry, Southern Illinois University, Edwardsville	Introductory	350	Biodiesel production from microalgae
Kevin M. Shea and David J. Gorin, Smith College	Introductory	16	Synthesis and bioactivity of anthelmintic neuroleptin analogs
Ratna Gupta, Our Lady of the Lake College	Introductory and Advanced	10 (Intro); 12 (Advanced)	Analysis of enzymes present in 'over-the-counter' supplements and fresh fruits/vegetables (Intro); Isolation and characterization of an enzyme present in bovine liver (Advanced)
Pamela Hanson and Laura Stultz, Birmingham-Southern College	Introductory and Advanced	12-20	Exploring the chemistry and biology of anticancer ruthenium complexes
Moriah R. Beck, Wichita State University	Advanced	24	Protein structure, function, and biochemical adaptation: Predicting the outcomes of amino acid substitutions at non-conserved positions
Louise K. Charkoudian and Robert Fairman, Haverford College	Advanced	16	Analysis and engineering of protein-protein interactions involved in natural product biosynthesis
Katherine L. Hayden, Birmingham-Southern College	Advanced	10	Isolation, purification and biophysical characterization of glycolytic enzymes in parasites for drug discovery in neglected tropical diseases and cancer

Kathryn L. Haas and Jennifer Fishovitz, Saint Mary's College, IN	Advanced	10-12	Investigating the mechanism of copper reduction by the human copper transport protein
Shahir S. Rizk, Indiana University South Bend	Advanced	12	Developing biosensors for the herbicide glyphosate using engineered mutants of a periplasmic binding protein
Alice Robson and Mark Dillingham, University of Bristol, UK	Advanced	25	Identification and characterization of putative prokaryotic ATPase enzymes
Penny J. Beuning, Northeastern University	Advanced	40	Enzyme function annotation in chemical biology
Jen Heemstra, Emory University	Advanced	60	Kinetics of bioconjugation using strain-promoted azide-alkyne cycloaddition
Jennifer A. Prescher, University of California, Irvine	Advanced	80-120	High-throughput drug screening using a luminescent cellular cytotoxicity assay
Linda Columbus, University of Virginia	Advanced	90	Known structure, unknown function (http://biochemlab.org)
Olalla Vázquez, Philipps-Universität Marburg	Advanced	20	A chemical biology approach to the epigenetics

The CUREs listed in Table 1 primarily emerged from the scholarly interests and teaching needs of individual faculty and have been implemented solely at their institution. In addition to these individual efforts, open source CUREs have been initiated, with the goal of engaging large cohorts of undergraduate students from around the world in research. For example, Science Education Alliance-Phage Hunters Advancing Genomics and Evolutionary Science (“SEA-PHAGES”; <https://seaphages.org>) and the Genomics Education Partnership (“GEP”; <http://gep.wustl.edu>) represent CUREs that bring together faculty and undergraduates from multiple institutions in pursuit of genomics-based research goals. Drugs for Neglected Diseases *initiative* (www.dndi.org) and Open Source Malaria (<http://opensourcemalaria.org>), are both open source CUREs aimed at pursuing new drugs to combat diseases that impact the developing world. These crowdsourcing opportunities align closely with the ideals of many undergraduates, as they offer the opportunity to contribute tangibly to global public health. And, since the projects come with established research design and well-defined goals, the barrier to implementation in the classroom is relatively low.

Across all institutional contexts and CURE formats, a key goal is to replicate at least some elements of the traditional research experience.¹⁰ To this end, CURE curricula can include instruction on research design and methods, and often engage students in reading of the primary research literature. These skills can be taught during the CURE itself, or during a pre-CURE course that is intended to prepare students for the open-endedness of the research experience. The outputs of traditional undergraduate research experiences can also be replicated in a CURE. Students may present their data in the format of a journal article or during a poster session, and there are examples of CUREs that produce publications in peer-reviewed journals with the students from the course listed as co-authors.¹³⁻¹⁸

It is important to note that because encountering unexpected outcomes is an inescapable aspect of research, it is highly likely that students in CUREs will experience “failed” experiments. For students who are acclimated to lab courses having prescriptive curricula and pre-defined experimental outcomes, adapting to the idea of ambiguity or short-term failure may require some coaching. The course instructor and teaching

assistants can facilitate this process by talking openly about the challenges that naturally arise as a part of the research process. Additionally, it is important that the student evaluation (i.e. grading) process focuses on conceptual understanding and effort, rather than success in specific experiments. Students may require frequent reassurance that unexpected obstacles are an inherent part of research, and will not negatively impact their grade in the course. The prospect of “unsuccessful experiments” may at first appear to be a drawback of CUREs. However, we argue that learning how to cope with perceived failure is a critical skill that will benefit students in their future careers, and CUREs offer an ideal setting for students to gain resiliency.

Community Resource (CoRe) projects enable students to make rapid contributions to scientific progress

In this new technological era of biochemistry, we see an opportunity to expand the impact of undergraduate work to digital contributions to online community resources (CoRes). CoRes are information/technology-based projects that create publically available products. CoRe projects represent an attractive class of CUREs because they are less resource intensive than laboratory-based CUREs, and the projects align with the expectations of today’s students to create products that are immediately viewable by a public audience.

Student contributions to bioinformatics CoRes

Existing biosynthetic repositories are being flooded with information, creating a need to make past and future information available in a standardized and systematic format.¹⁹ Moreover, as the field of biochemistry continues to converge disciplines, the siloed nature of existing repositories creates an additional challenge for scientists. As such, there is an emerging need to deploy resources to tackle data annotation and organization in order to prevent researchers from drowning or getting lost in their own data.

These unmet needs within the field of biochemistry present opportunities to engage students in meaningful research while learning about bioinformatics and enzymology. For example, in 2008 a distributed grid of 515 undergraduate students conducted detailed functional and phylogenetic analyses to annotate metagenomics sequences.²⁰ The student-generated results proved to be surprisingly reliable after validation. The course has now been run by dozens of student teams from a wide range of universities based on the Annotathon online training environment (<http://annotathon.org/>), and an open course with 1,291 students is currently under way. The Annotathon project shows promise in making contributions to the field of biochemistry, as a similar project lead to the discovery of a reductase that decreases triclosan susceptibility in *Escherichia coli*.²¹ The engagement of large numbers of students is powerful because it allows leveraging the ‘wisdom of the crowds’.²² Notably, whereas citizen-science crowdsourcing of bioinformatics challenges often suffer from participants paying transient interest,²³ this is not expected to be an issue for bioinformatics-based undergraduate CoRe projects. Undergraduate students tend to remain productive due to their dedicated time on task and motivation to complete a project that is part of a course.²²

The ‘wisdom of the crowds’ was also exploited in a CoRe project focused on the standardization of data on fungal gene cluster involved in the biosynthesis of natural products.¹⁵ While these gene clusters were described somewhere in literature, information was not readily usable because the data were published prior to the

establishment of the Minimum Information about a Biosynthetic Gene cluster (MIBiG; <https://mibig.secondarymetabolites.org>) standard.¹⁹ The MIBiG standard facilitates consistent annotations of such gene clusters to be deposited to an online, freely accessible, and computer-readable repository by researchers upon submitting a paper. In a CoRe project, undergraduate students had the opportunity to make a major contribution to scientific progress: a panel of 19 students analyzed 275 research papers, which led to the detailed annotation of the genetic basis for the biosynthetic pathways of 128 natural product families. In the end, the results allowed for a detailed analysis of the phylogenetic distribution of known and unknown fungal biosynthetic pathways. The products of this CoRe project offered clear direction to experimental research aimed at the discovery of novel fungal natural products.

In general, many annotation problems at the interface of biochemistry and bioinformatics are amenable to such CURE approaches, as they allow students to practice coupling bioinformatic tools with detailed biochemical interpretation and discovery. In principle, these efforts could even be organized within massive online open courses (MOOCs), as long as the learning experience is thoughtfully integrated into the work the students perform. Bioinformatics CoRe projects implemented through MOOCs could involve thousands of students worldwide and enable data analyses on a scale and with a quality unattainable either by research groups or by automated efforts.

Student contributions to pedagogical CoRes

As technology continues to play a central role in the way in which students and experts access and learn new information,²⁴⁻²⁷ there will remain an ongoing demand for the development and maintenance of web-based and open-access pedagogical resources. Like the data repositories discussed above, open-access knowledge-sharing platforms benefit from the “wisdom of many” paradigm while creating the need for contributions and maintenance from the many.²⁸ These growing needs provide opportunities for faculty and students to create and share knowledge resources with the broader community through CoRe projects. Table 2 highlights three specific examples of digital open access information platforms that are amenable to contributions through CoRe projects: Wikipedia (www.wikipedia.org), YouTube (www.youtube.com), and LibreTexts (née ChemWiki; <https://chem.libretexts.org>).

Table 2: Example CoRe projects in three digital platforms.

Information Platform	CoRe Project	Benefit to Community	Student Gains	Example
YouTube	Students develop new educational videos about chemistry topics or laboratory techniques.	Expansion of publicly available educational video library.	Learn to use software, produce images, edit video, become aware of accessibility issues, develop communication skills, in-depth learning of topic.	29,30
Wikipedia	Students edit existing articles or create new articles, design and create original figures.	Increased access to information, increased clarity of information, expansion of public information library.	Digital/information literacy, critical research, teamwork, writing skills, writing for a public audience, in-depth learning of topic.	31
LibreTexts	Students develop a new article on a topic including figures and linked to external	Increased access to information, increased clarity of information,	All of the above.	30

	resources like YouTube videos or 3D print files.	expansion of open-access pedagogical resources.		
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Classroom CoRe projects that focus on contributing to digital educational resources enable students to develop skills in information literacy, critical research, teamwork, and technology.³² To engage students in contributing to open-access knowledge resources through course projects, Wikipedia established the Wiki Education Foundation (teach.wikiedu.org).^{27,33} The barriers to integrating Wikipedia projects into coursework are decreased significantly by the support that Wiki Ed provides to students and faculty who formally participate in classroom projects. Instructors are provided with a course dashboard for managing student assignments and training modules to help students learn about Wikipedia's standard of conduct. Access to dedicated Wikipedia experts (Wikipedia Ambassadors) further facilitates student editing and content generation. In the Fall semester of 2016, more than 6,000 students in 270 courses across all disciplines, including biochemistry, contributed to Wikipedia through CoRe projects.²⁷

Alternative digital venues for CoRe projects include LibreText (a free, interdisciplinary, and customizable online textbook)³⁴ and YouTube. As a specific example of a YouTube CoRe project, students in a laboratory-based CURE were challenged with the task to make a video to teach a technique used within the course; a video they wished they had as a resource before or during the course to help them learn this technique.³⁰ The students created videos on topics ranging from correct micro-pipetting to determination of metal-peptide affinity constants. The videos are posted on YouTube for use by the general public and these YouTube videos are linked to the course management site so that they can be used by future students enrolled in the course.

In an example of a classroom CoRe project utilizing both YouTube and LibreText, students completed comprehensive literature research and writing assignments for public dissemination on both platforms. Eight students enrolled in the course chose a topic selected or approved by the instructor, on which they would build several resources over the semester. Students worked individually to produce original figures, a narrated molecular animation video, and a 3D-print file, in addition to a written article. Students produced several drafts of each product and were provided formative assessment with the goal of producing high-quality "publication-worthy" materials. Five out of eight projects met this requirement. Publication-worthy videos were posted to YouTube and were made accessible to diverse audiences by including student-generated transcripts. These videos, as well as corresponding figures and writing, were posted on LibreText in a chapter of the course's digital textbook. Less than one year later, the five student-generated videos have received over 3,000 cumulative views on YouTube.

Advantages of CURE and CoRe projects.

What CUREs and CoRe activities have in common is that they engage students and faculty in meaningful work that is useful to a broader community outside of their classroom or laboratory. In this way, CUREs and CoRe projects are research-like enterprises that provide students with some of the same advantages that have been documented for students and faculty engaging in undergraduate research endeavors.³⁵ Additionally, these course-based activities are intrinsically project-based and active learning practices which increase student buy-in and improve student performance,

learning, and skill development.^{36,37} Several distinct benefits of CoRe projects include: i) the work can be accomplished in the context of classroom seminar-style courses, ii) student products are made available on the timescale of the course (rather than after multiple years, which is more common for CUREs leading to publications), iii) cost is relatively low compared to laboratory-based CUREs, and iv) students gain an immediate and tangible sense of contributing to the greater good. Moreover, in general, today's students are technology enthusiasts, and are eager to learn from, and contribute to, online resources.

Advantages for student learning and future success: A growing body of evidence demonstrates that CUREs and CoRe projects increase students' learning while simultaneously increasing their engagement and satisfaction with course assignments.^{10,11} Students involved in course-based activities like those discussed above report that they value assignments, are more proud of their work, spend more time on assignments, and learn more digital literacy and writing skills compared to traditional course assignments.²⁷ Many of today's students desire to understand the application of skills and knowledge before investment in learning, and therefore it is not surprising that these students value CUREs and CoRe exercises more than traditional course assignments (e.g. traditional writing assignments, cookbook laboratory experiments).²⁷ The generation of content for an public audience makes students members of the scholarly community and helps them recognize the tangible benefits of their work to this broader community. These course activities also produce skills that help students succeed in their life, scholarship, and careers. In our own experiences, students report that their experiences with CURE and CoRes helped them find clarity of purpose in their career path, increased their problem-solving skills and tolerance to failure, and strengthened their confidence.^{17,38,39}

Advantages for faculty: Faculty are more satisfied with their work when it is meaningful and when their students are both productive and happy. Aside from general satisfaction with their teaching activities, CURE and CoRe projects can enhance the faculty member's scholarly activity.¹¹ As faculty are pulled in many directions, the consolidation of faculty teaching and research efforts is critical to sustainable success. If faculty can accomplish high-impact teaching in the same activities which provide research momentum and/or contribute to local or broader community through CUREs and CoRe projects, it is a more efficient use of faculty resources compared to siloed efforts. Through CoRe courses, faculty can also leverage student time to accomplish improvements in pedagogical materials, which not only improves their own course resources, but provides resources for other faculty and students in and outside of their own institutions.

Advantages for institutions and the community: The outcomes of research-like course activities discussed here are in line with the missions of higher education institutions and serve both the institutions and the broader community through satisfying students, faculty, donors, and the community. When faculty and students engage in CUREs and CoRe projects, they are more satisfied with their teaching and learning, leading to increased retention of both students and faculty. Active-learning and research-like practices especially increase the engagement, retention, and success of underrepresented minorities and women in STEM fields compared to traditional laboratory or lecture courses.^{36,40-42} Thus, CUREs and CoRe activities benefit institutions and society by attracting and retaining diversity in STEM. Further, CUREs

and CoRe products like research articles, database annotations, and pedagogical materials are visible examples of excellence in teaching, scholarship, and service at an institution. These products can be used to advertise the excellence of an institution's scholarship and teaching for the purpose of recruiting students and in fundraising.

High-quality products of CUREs and CoRe projects benefit the community by making information publicly accessible. In 2008, the Higher Education Opportunity Act called for an alternative to high-cost textbooks that impede access to education for students with limited financial resources. By answering this call, the products of CoRe projects can make education more accessible to all students.⁴³

Assessing the value of CURE and CoRe projects

As CUREs gain traction in colleges and universities worldwide, there is a growing body of resources to aid in assessing the benefits of these activities to faculty, students, and the progression of research. Contributions of CoRe projects to the field of biochemistry can be in part measured by metrics, such as the number of entries into a particular biochemical database, or the number of views of educational materials. In terms of student growth, a recent article provides a practical guide for assessing CUREs, highlighting over thirty different strategies that can be employed by instructors.⁴⁴ Many of these strategies are amenable to the assessment of undergraduate-led CoRe contributions, basing the selection of a particular tool on the primary goals of the exercise. These resources, as well as customized surveys and reflective student portfolios,⁴⁵ can be combined to achieve a holistic approach to assess the outcomes of CURE and classroom CoRe projects. Instructors are encouraged to assess their own experience as well to evaluate how CUREs and CoRe projects impact their teaching and scholarly work.

Challenges and Opportunities

While there is strong evidence that CUREs bring significant benefits to both students and faculty,¹¹ change often meets resistance.⁴⁶ Common barriers to implementation include fiscal constraints, pressure from institutional culture and tradition, time investment, and logistics. While the time and effort required to establish and maintain a CURE/CoRe varies by topic, we have found that the success of any CURE/CoRe depends on entering into the course with all requisite materials prepared, a clear vision, an organized plan of attack, a handful of backup plans, and a flexible attitude. It also helps to define in advance how (and when) the student-generated data will be curated, vetted, refined, and written up for public dissemination.

In order to readily assess student-generated data, we recommend that faculty incorporate CUREs or CoRe projects related to their scholarly work such that they can appropriately assess the outcome of student efforts. In the case of contributing to online repositories such as MiBIG, one can reduce faculty workload by introducing an element of random redundancy such that each annotation is assigned to two or more students. Any entry supported by all independent students can be viewed as confirmed, thus reducing the number of entries that need to be manually examined by an expert. This sort of approach has been utilized successfully in the past in the undergraduate-led curation and analysis of fungal gene biosynthetic gene clusters of published natural products described above as well as various other studies.^{15,20,47}

One model for overcoming the burden of time and effort required to establish and maintain a CURE/CoRe project is to incorporate either the development or completion of the project into undergraduate senior thesis or summer research. In this context, individual undergraduates can build foundations for projects that can be deployed in CURE/CoRe environments, or can focus their efforts on curating data from a previously implemented CURE/CoRes to bring a project to completion. These projects can be particularly rewarding for students with interests at the intersection of science and education.

The impact and importance of CUREs in chemistry was recently the focus of a National Science Foundation funded think tank, which highlighted benefits of incorporating biochemistry CUREs on the institutional level.⁴⁶ These benefits—which include increasing graduation rates, broadening inclusion of students to build a more diverse community, increasing research productivity, and building institutional reputations—should provide fodder for institutional buy-in. Fiscal and temporal support from institutions and funding agencies will undoubtedly play a critical role in the future of CUREs in biochemistry. For those who are interested in incorporating original research in the classroom but limited by financial constraints, an attractive path forward could be focusing on digital contributions to community resources through CoRe projects. The bioinformatics and pedagogical CoRe projects described above do not require funds to implement. Moreover, they can be implemented in a diverse range of settings, including lecture-, seminar- and lab-style courses.

Summary and Outlook

We hope that by sharing stories about CUREs and CoRe projects, these methods of teaching will be adopted by those interested in collaborating with undergraduates in new ways, and thus impacting the future of biochemistry through this type of coursework. For support in incorporating CUREs into practice, we point the reader to CUREnet (<https://curenet.cns.utexas.edu>), a network of people and programs that are creating CUREs in biology, the Center for the Integration of Research, Teaching and Learning (<https://www.cirtl.net>), the CURE FaceBook community, and recent publications and pamphlets.^{46,48,49} Faculty listed in Table 1 also agreed to be available to discuss their projects and share materials. For those interested in the CoRe projects mentioned above, in many cases information on how to get involved can be found on their respective websites. The corresponding authors of this *Perspective* are also available to facilitate initiating a new, or collaborating on existing, CoRe projects. While the time it takes to develop and execute a CURE or CoRe project can be daunting, faculty who have made this investment report that is worth it—they find increased enjoyment and productivity in their work.

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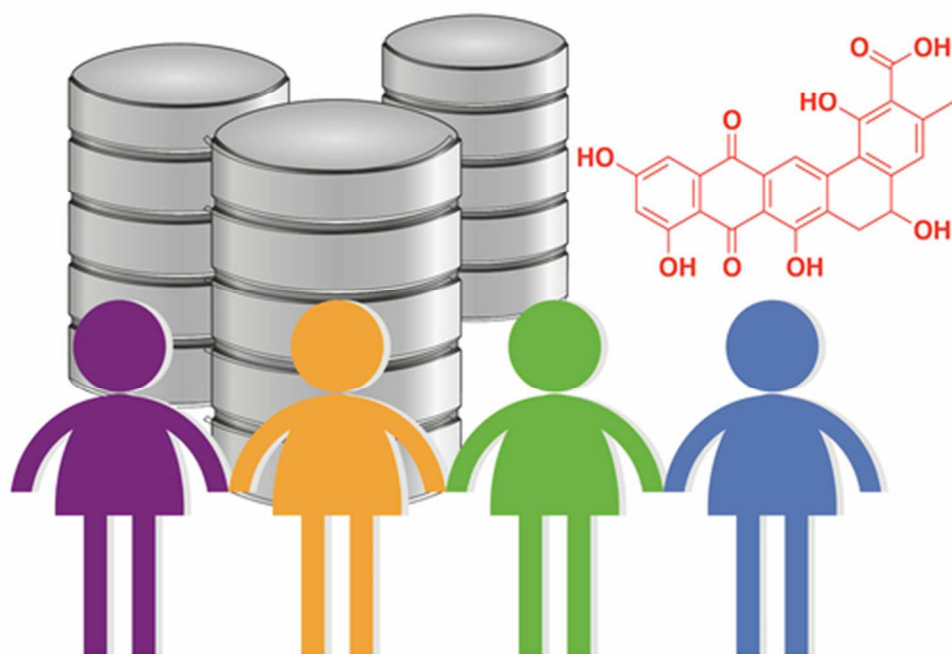
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