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Understanding Differences in Underrepresented Minorities and First-Generation Student Perceptions in the Introductory Biology Classroom

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We used quantitative methods to better understand the perceptions of students in an introductory biology course (Biology 101) at a small, liberal arts college (SLAC) that is also a primarily white institution (PWI). In pre/post surveys, we asked students questions related to their attitudes and beliefs about their professor, classmates, and Biology 101. We were especially interested in the responses and outcomes of underrepresented minorities (URM) and first-generation (FG) students. Our findings suggest URM and FG students have a decreased sense of belonging and increased perceptions of exclusion and differential treatment due to race. These findings can explain, in part, the disparity in Biology 101 grade and STEM (science, technology, engineering, and math) attrition.

KEYWORDS introductory biology, underrepresented minorities, first-generation, perception, attitude, survey, disparities, stereotype threat, kindness cues

INTRODUCTION

Diversity benefits society through increased financial returns, fostered innovation, objectivity, and greater problem-solving ability (1–4). Unfortunately, in STEM (science, technology, engineering, and math) diversity decreases as people from underrepresented minorities (URM) groups leave as they progress from enrollment in postsecondary institutions to graduation and finally to occupations in science (<https://nces.nsf.gov/pubs/nsf19304/assets/data/tables/wmpd19-sr-tab09-007.xlsx>; 5–7). Attrition of people from URM groups occurs even as STEM jobs are increasing. This disparity leads to exclusion from growing and high-paying careers, a continual shortage of qualified job seekers, and loss of innovation in STEM fields and is financially detrimental to URM individuals, as STEM jobs earn 29% more than non-STEM jobs (8, 9).

Loss begins early in postsecondary education and continues throughout. URM students start college declaring a STEM

major at comparable rates to non-URM students; however, they graduate in STEM majors at much lower rates (10, 11). About 20% of Native Americans, black, and Latino students complete their STEM degrees while about 33% of whites and 42% of Asian-American students complete their STEM degrees in 5 years (12). Systemic and programmatic culture barriers reported by URM students include negative experiences (e.g., stereotype threat, feelings of isolation, competitive climate, perceived discrimination), loss of confidence due to low grades, inadequate financial aid, challenges with large, lecture-style courses, and lack of mentorship/institutional support (13–17). The effect of these barriers is demonstrated by the persistence of exam score and course grade disparities between URM and not-URM students even when prior academic performance is controlled (10, 18–22).

Evidence from successful interventions also supports the conclusion that much of the difference in student success is due to nonacademic considerations such as programmatic culture and living in a racist society. For example, interventions involving cognitive work to reinforce students' sense of their own value, that they belong, or that they do not need to serve as a representative of their race all contribute to greater success in STEM courses (23–26). Students' sense of belonging is determined by whether they perceive that their contributions to the classroom environment are accepted, included, and valued by others (instructors and peers). This determines whether the student feels they are an important part of the activity and energy of the class (27).

Steele and Aronson first described the concept of stereotype threat as a systematic barrier to URM students (28).

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Stereotype threat is the anxiety that an individual's poor performance will confirm a negative stereotype and thus undermine that individual's performance (28, 29). Due to the legacy of discrimination in the United States and in institutions of higher learning, URM students are often aware of the negative stereotypes that their peers or professors may hold. This creates the expectation that their treatment is contingent on their URM status (13, 30). Increased self-consciousness based on an individual's identity contingencies reduces an individual's perceptions of their own efficacy, lowers confidence and sense of belonging, impacts biological responses such as blood pressure, and overall, negatively affects the ability of an individual to learn (31–35). Interpersonal cues or instructor immediacy, such as smiling or avoiding eye contact, play a role in the classroom environment and affect students' sense of belonging (14, 36–38). Interpersonal cues are founded on the norms of the traditional majority groups and may be negatively interpreted, resulting in stereotype threat that adversely affects a student's sense of belonging, which can negatively impact student performance and lead to attrition from STEM majors (11, 13).

Research about minoritized and first-generation (FG) students in STEM courses has primarily been done at large, typically urban R1 institutions and community colleges (10, 20, 39). Our work focuses on small, liberal arts colleges (SLAC). This research was done at a primarily white institution (PWI) in a rural environment. SLACs differ from R1s in important ways. For example, introductory biology class sizes at R1 institutions are often 150 students or more. At the institution studied, introductory biology classes average fewer than 30 students. Small class sizes combined with small proportions of URM students in Biology 101 make it unlikely that URM or FG students will have a classmate that shares their identities. Our goal was to have a better understanding of how URM students, FG students, and students who are both URM and FG perceive their classmates, professor, and overall experience in Biology 101 at these sorts of institutions.

We selected Biology 101, the first course students take in biology, for several reasons. Introductory biology is a “gateway” course usually required for students to major in many STEM disciplines as well as most health care-related professional programs. At the institutions where we conducted our research, about 40% of all first-year students take Biology 101 during their first semester. Much of STEM attrition occurs during or at the end of the introductory course sequence and can be linked to poor performance in the introductory courses (18, 40). A better understanding of URM and FG students' experiences in Biology 101 could lead to changes that address structural and programmatic issues negatively impacting URM and FG students' experiences and academic outcomes.

The research questions compared four student groups—URM and FG, URM and not-FG, not-URM and FG, not-URM and not-FG. We had two research questions: (i) how do course grades and persistence in STEM majors differ between these groups and (ii) how do attitudes and perceptions about biology, professors, and classmates differ between groups? Based on previous work (41, 42), we hypothesize that students who identify

as both URM and FG would have the lowest course grades and persistence and have more negative attitudes and perceptions about biology, their professors, and their classmates. They would be followed by URM, then FG, and last, not-URM and not-FG students.

METHODS

This research was carried out at a 4-year private liberal arts college located in a rural area in the Midwest. The total undergraduate population is approximately 3,200 students, with 17.2% identifying as U.S. students of color, 3.4% being international students, and 26% identifying as first-generation. The institution has a 4-year graduation rate of 76%. During the fall semester of 2018 and fall semester of 2019, there were 27 sections of Biology 101 lecture taught by 13 distinct instructors, with an average class size of 29.

This study included three parts—institutional data on registered students (registrar data), a voluntary, anonymous, online survey of student attitudes given in the first 2 weeks of class (pre-survey), and a similar survey of student attitudes given in the last 2 weeks of class (post-survey). Demographic data can be found in Table S1 in the supplemental material.

Registrar data ($n = 785$) included fields for ethnicity, first-generation status, binary gender, test scores, high school GPA, instructor, data on further biology courses taken, and sufficient data to calculate GPA-other (GPAO). GPAO reports the GPA for courses taken concurrently with Biology 101. Registrar data were the source of all GPA and test score-related data (Fig. 1, Tables 1 and 2, Tables S1 to S3). The supplied data did not include personal identifiers, so direct connection with the survey data was not possible. ACT Math was 93% complete, but in 5% of cases, missing ACT Math could be converted from SAT Math (assuming post-2016 SAT); in 2% of cases neither was available. Registrar data were complete for ethnicity, first-generation status, and binary gender. Additional registrar data ($n = 837$) on the graduation outcomes of Biology 101 students from the fall semesters of 2015 and 2016 were used for Fig. 3.

The surveys included Biology 101 students in the fall semesters of 2018 and 2019. Pre-survey ($n = 486$, 62% response) demographic questions included high school science courses taken, current major, and attitudes about biology. The post-survey ($n = 391$, 50% response) repeated pre-survey questions and included 17 additional questions with Likert scale responses assessing student perceptions of classmates, professors, and Biology 101. The pre-survey and post-survey responses were collected anonymously, which prevented direct individual comparison of pre- and postcourse responses. Surveys are the source of data on student experiences and attitudes (Fig. 2, Fig. S1, Table S4). Survey questions using Likert scale responses were more than 98% complete.

For consistency, we use URM and FG language throughout the paper. However, since the surveys used self-identified demographics and were not connected to institutional measures, survey measures of ethnicity and first-generation status are different from

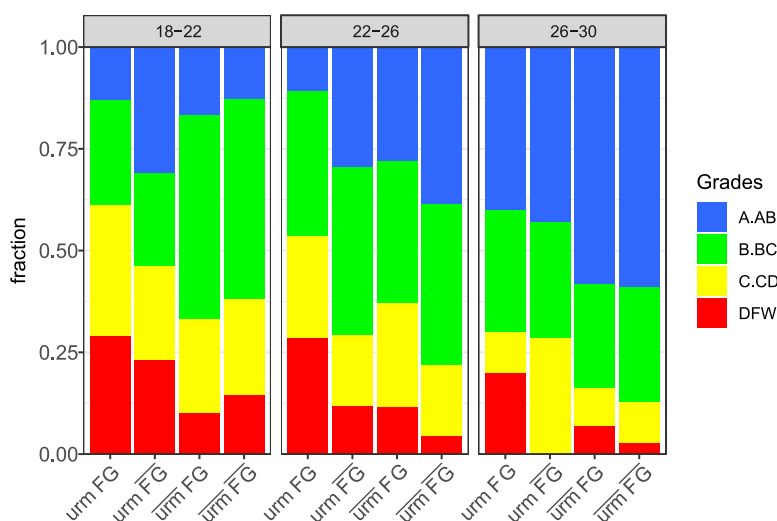


FIG 1. Distribution of Biology 101 grades by group and ACT Math score from registrar data. Each facet displays students with ACT Math score in various intervals (e.g., 18–22). *urm* (FG) denotes the not-URM (not-FG) groups. The institution’s grading system inserts grades AB, BC, and CD as intermediate grades between the usual A, B, C, and D grades; W denotes a withdrawal, and F, failure. The number of students for each column from left to right are 31, 13, 30, 55, 28, 17, 43, 182, 10, 14, 43, 180.

the institutional measures reported by the registrar. Ethnicity data from the Registrar was trinary (white, American student of color [ASOC], Intl); the international students were dropped. When registrar data are used, the American students of color (including Asian, black or African American, Hispanic of any race, American Indian/Alaska Native, two or more races, Native Hawaiian/Pacific Islander) are labeled in this paper as URM. Students are labeled as first generation in registrar data if neither parent completed a college degree (based on student self-reports). As noted in their captions, Fig. 1 and 3, Tables 1 and 2, and Tables S1 to S3 use registrar data. Students in the surveys were identified as URM if Black or Hispanic was selected. Students in the survey were identified as first-generation if they answered yes to the question “Are you the first person in your family to go to college?”. As noted in their captions, Fig. 2, Fig. S1, and Table S4 use survey data. In all, 7 students did not report a race/ethnicity; 15 did not report FG status. In these surveys both URM and FG status are underreported compared to the registrar data.

Questions analyzed in Fig. 2 and Fig. S1 and found in post-survey question 16 in the supplemental material were either based on prior surveys or inspired by our research questions and

literature on stereotype threat and sense of belonging. The questions about Biology 101 were modified from Harackiewicz et al. and Wilson et al. to make them specific to this course (43, 44). Questions asking whether their identity contingencies of race or gender affects how their classmates or professor thinks about them were inspired by our research questions, literature on stereotype threat and sense of belonging, and a panel of students of color from the institution (<https://www.youtube.com/watch?v=M773AoyOIZA>).

Analysis was conducted in R (45), and figures were produced using the packages ggplot2 (46) and Treemap (47).

All parts of the study, including the informed consent process and confidentiality parameters, were reviewed and approved by the Institutional Review Board (IRB). Safety issues are not applicable to this type of research.

RESULTS

Biology 101 grade disparities persist even when ACT math scores are controlled

URM and FG students receive lower grades than majority groups, with an additive effect for students that are both (Table 1).

TABLE 1

Comparison of Biology 101 grade for students enrolled the fall semesters 2018 and 2019 from registrar data^a

Student category	No.	Avg	SD
URM FG	86	2.06	1.06
URM not-FG	52	2.59	1.16
Not-URM FG	136	2.79	1.06
Not-URM not-FG	496	3.07	0.93

^aThe institution’s grading system is based on A = 4.0, AB = 3.5, B = 3.0, etc. The grade distributions are significantly different ($f = 27.9, P < 0.001$).

TABLE 2

Ordinary least square regression table for Biology 101 grade using ACT Math, URM, and FG from registrar data^a

Coefficient	Coefficient	SE	T	P value
(Intercept)	0.402	0.223	1.8	0.073
ACT Math	0.106	0.009	12.2	<0.001
URM = true	-0.329	0.094	-3.5	<0.001
FG = true	-0.184	0.078	-2.4	0.018

^a $R^2 = 0.24, F = 82.3, P < 0.001$.

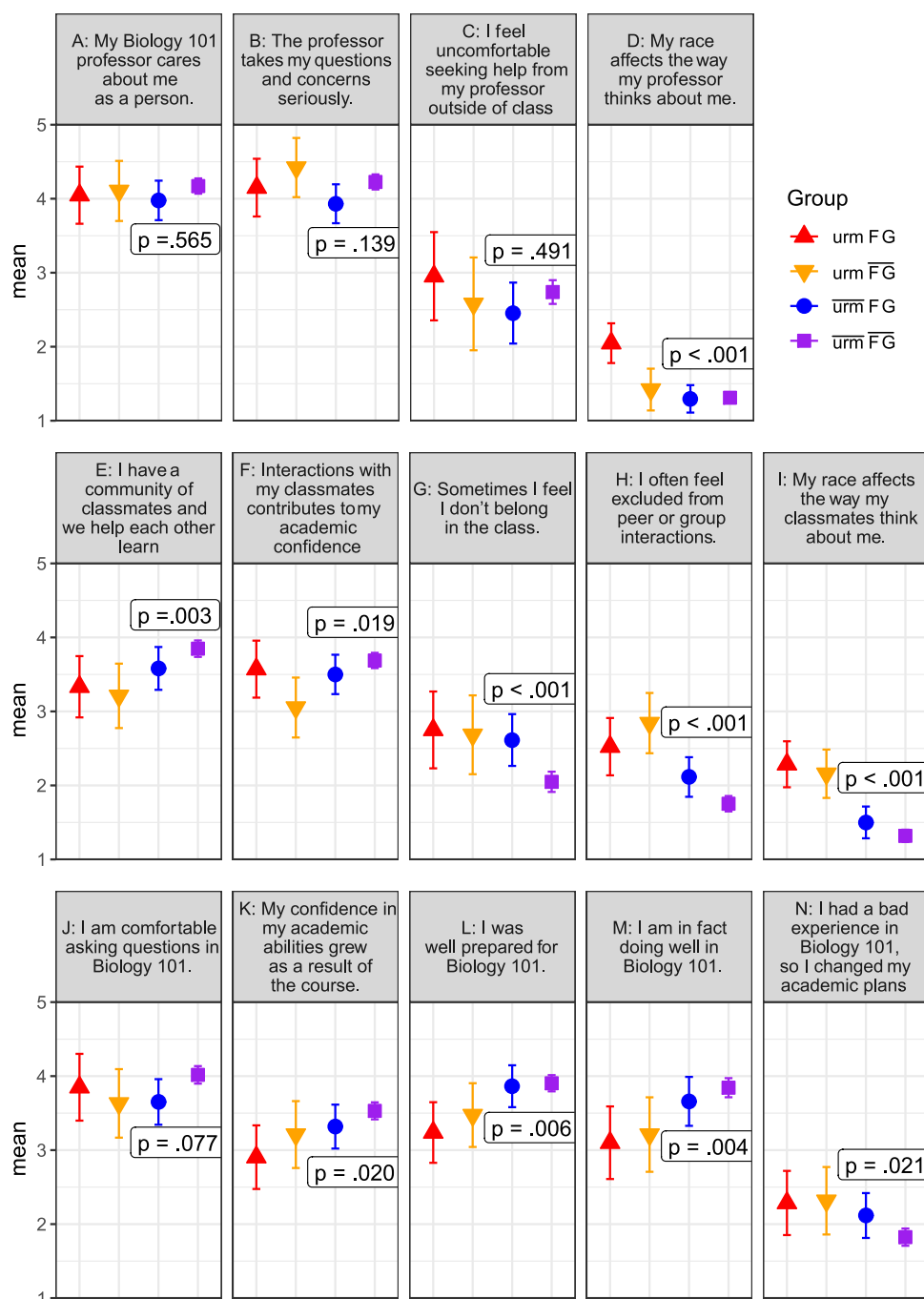


FIG 2. Mean and 95% confidence intervals for post-survey questions by group; 5 = strongly agree and 1 = strongly disagree. $\overline{urm} \overline{FG}$ denotes the not-URM not-FG groups. ANOVA was used to calculate P . The mean and standard deviation for these data can be found in Table S4.

We found no significant difference between groups in the total number of high school science classes taken or in completion of an AP (or advanced) high school biology course. Nevertheless, in the pre-survey URM and/or FG students responded to the question “I am well prepared for Biology 101.” significantly more negatively (analysis of variance [ANOVA], $F = 4.6$, $P = 0.003$; Fig. S1).

URM and FG students had significantly ($F = 34.8$, $P < 0.001$) lower ACT Math scores (Table 2), which if taken as a measure of preparedness, might explain the grade disparity. However, when students with similar ACT Math scores are compared,

differences in Biology 101 grade remain as illustrated by the largely diagonal pattern of Fig. 1. At this institution grades are assigned on a 4.0-point scale, with intermediate grades at each halfway point (AB=3.5, BC=2.5, CD=1.5; there is no DF grade). Figure 1 shows that despite being grouped by ACT Math score, URM and FG students receive more D, F, and withdraw (DFW) grades and fewer As or ABs. In the 18 to 22 ACT Math range the number of students receiving an A or AB does not follow this trend, but the number of URM and FG students is small ($n = 13$).

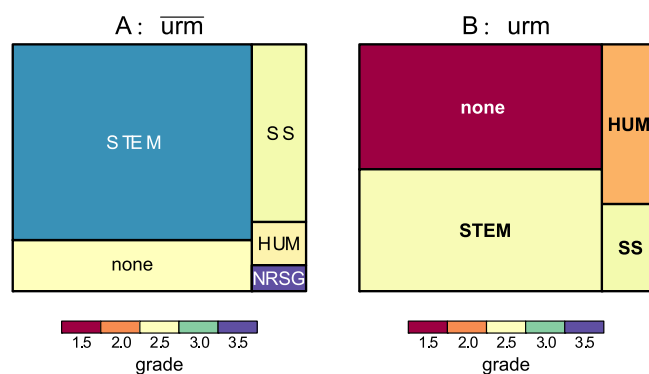


FIG 3. Registrar data reflecting persistence of Biology 101 students from 2015 to 2016 who began Biology 101 intending to complete a STEM major by group (A, not-URM; B, URM). The relative size of the boxes displays the proportion of those students that by 2020 earned a degree in the particular areas (SS, social science; HUM, humanities; NRSG, nursing; STEM, science, technology, engineering, mathematics; none, no degree obtained), and boxes are colored by the average Biology 101 grade of each group. The degree-success and grades of URM students are less than those of not-URM students. The outcome disparity between URM and not-URM is quite significantly different as measured by a 2×6 Fisher exact test ($P < 0.001$). \overline{urm} denotes the not-URM group. Note that disaggregation into our usual four groups results in very small cell counts; details can be found in Table S2.

A linear model was built predicting the numerical Biology 101 grade based on URM status, FG status, and ACT Math score; all the coefficients (Table 2) were significant, with URM status reducing the Biology 101 grade by about 0.3 and FG status reducing grade by about 0.2. Interaction terms, when included, were not significant. Interestingly, if we controlled for preparedness using GPAO instead of ACT Math score, only FG status remained significant. Apparently, URM-status effects are approximately equally present in both GPAO and Biology 101 grade; indeed, the difference between Biology 101 grade and GPAO does not differ significantly based on URM status (t test, $t = -1.3$, $P = 0.19$). We conclude that these preparedness measures cannot explain all the grade disparity.

We noted that in the pre-survey the groups differed in their evaluation of how well prepared they were for Biology 101 (Fig. S1); however, in almost every other pre-survey measure (e.g., concern for community, environment, helping people, the nature and importance of Biology 101 for them), they did not differ significantly.

Biology 101 students respond similarly to survey questions about the professor

Previous work suggests that feelings of belonging and sense of community are important factors in student success. Professors play an integral role in establishing, supporting, and perpetuating the classroom environment (24). Students from all examined groups had a positive perception that the professor cares about students and takes their questions and concerns seriously (Fig. 2A and B). Previous work has suggested that FG students may not feel comfortable asking a professor for help outside class (48). That does not appear in our work (Fig. 2C).

For the three professor-related prompts, there were no significant differences in responses between student groups. While students that are both URM and FG generally disagree that their race affects the way their professor thinks of them, they have a weaker disagreement resulting in a significant difference ($F = 9.3$, $P < 0.001$) in their response (Fig. 2D). This is especially notable for URM FG students.

Perceptions of classmates are significantly different

While the professor was often viewed similarly by the groups, there were significant differences in the perceptions of classmates. URM FG, URM not-FG, and not-URM FG students feel significantly ($F = 5.9$, $P < 0.001$) less belonging in the classroom compared to not-URM not-FG students (Fig. 2G). This feeling is mirrored by these same groups feeling significantly ($F = 13.6$, $P < 0.001$) more excluded from peer or group interactions (Fig. 2H). Feelings of exclusion and lack of belonging could be the result of peer racial attitudes. URM students disagree significantly ($F = 18.6$, $P < 0.001$) less strongly that their race affects the way their classmates think about them (Fig. 2I). In line with these perceptions of their classmates, we find (Fig. 2E) that URM students agree significantly ($F = 4.7$, $P = 0.003$) less strongly that they have a community of classmates that help each other learn. Interestingly, URM FG students respond (Fig. 2F) similarly as not-URM FG and not-URM not-FG students to the feeling that interactions with their classmates contribute to their academic confidence. However, URM not-FG students agree significantly ($F = 3.4$, $P = 0.019$) less strongly to that statement.

Attitudes about the Biology 101 course are different

Feelings and perceptions about the professor and classmates can impact attitudes about the Biology 101 course. There was no difference between groups about their comfort in asking questions in Biology 101 (Fig. 2J). URM students at the end of the semester felt significantly ($F = 4.2$, $P = 0.006$) less prepared and agreed significantly ($F = 4.5$, $P = 0.004$) less strongly that they were doing well in Biology 101 (Fig. 2L and M). These differences in student perceptions are echoed in the grade outcomes discussed in Fig. 1 and Table 1. URM FG, URM not-FG, and not-URM FG agreed significantly ($F = 3.3$, $P = 0.020$) less strongly that their confidence in their academic abilities grew because of the course (Fig. 2K). Together, these student perceptions culminate with URM students disagreeing significantly ($F = 3.3$, $P = 0.021$) less strongly with the statement “I had a bad experience in Biology 101, so I changed my plans” (Fig. 2N). Interestingly, in both the pre- and post-surveys the groups did not differ significantly in their assessment of the “subject of Biology” as interesting, useful, hard, or fun.

Disparities in persistence and graduation

Based on our earlier results, we asked if differences in student attitudes of academic preparedness, experiences in Biology 101, and grades would be echoed in student persistence.

To focus on STEM persistence, we used registrar data from the fall semesters of 2015 and 2016 to determine the graduation status 4 and 5 years after Biology 101. In Fig. 3 the previously discussed grade disparity is immediately evident, but here, we focus on the persistence gap; 66% of not-URM STEM students completed a STEM or nursing degree (Fig. 3A); only 40% of the URM students did (Fig. 3B), a highly significant difference (Fisher exact test, $P < 0.001$). In addition, 17% of not-URM STEM majors had not completed a degree at the institution by the end of the fall 2020 semester; 41% of the URM STEM students completed no degree, a highly significant difference (Fisher exact test, $P < 0.001$). For comparison, during this same period 31% of URM students who did not take Biology 101 did not complete a degree. The data in Fig. 3 were not disaggregated, for reasons discussed in Table S2.

If we look at STEM persistence as a function of Biology 101 grade, we find that for grades above C, the STEM-persistence of URM is consistent with not-URM. For grades C and below, URM's STEM persistence rate was just 62% of that for similar not-URM. Equal persistence rates for this group are near the edge of the 95% confidence interval for disparate impact (one-sided Fisher exact test, $P = 0.046$). We performed a linear logistic regression and found that the only significant predictor of persistence was Biology 101 grade (Table S3). It appears that URM and/or FG status do not lead directly to a decrease in persistence. Rather, URM and/or FG status result in lower Biology 101 grades (Table 1), and students with lower Biology 101 grades have decreased persistence (Fig. 3).

DISCUSSION

While there are many reports (10, 20, 39) on outcome disparities at R1 institutions and community colleges, relatively little work has been done on outcomes and experiences for URM and FG students at small liberal arts colleges (SLAC) that are also a primarily white institution (PWI). We were interested in how small class sizes, the rural setting, and the small proportion (18%) of URM students in the biology classroom would affect student outcomes, perceptions, and experiences.

Providing context for STEM attrition

The STEM attrition and grade disparities (Table 1 and Fig. 1) reported here are consistent with other reports from R1 and community colleges (10, 11, 17, 23). In this study, the differences in persistence are most strongly related to grade (Table S3), and student grades are significantly affected by URM and FG status (Table 2). We also found that URM and FG status correlates with perceptions of a more negative classroom environment (Fig. 2). We see that URM students begin Biology 101 feeling less prepared than not-URM students (Fig. S1). This feeling is carried through the semester; as URM students surveyed during the last 2 weeks of Biology 101 are less likely to agree with the statement "I am in fact doing well in Biology 101." (Fig. 2L). This feeling of doing less well is apparent in the registrar data

showing that URM students have significantly lower grades in Biology 101, even compared to those with the same ACT Math score (Table 1 and Fig. 1). And many of the students with low Biology 101 grades do not complete a degree (Fig. 3). While our data can only indicate correlation, if the reduced GPA for URM FG students were eliminated, the odds ratio for completing a degree would rise by a factor of 1.5 (Table S3). In our data, this would mean that rather than 62% of these students graduating compared to other students, 82% would be predicted to graduate. This is consistent with prior work showing that an increase of first-semester GPA from 2.5 to 3.5 led to a 1.80 increase in the odds of persistence for FG students (17).

Contributors to differing perceptions and attitudes in students

Our research provides context for these outcome disparities. Our survey about feelings, perceptions, and attitudes is a window into our students' experiences. One major finding from this work is that URM status was the largest factor contributing to differences in perception and attitudes, while FG status had an additive effect in some areas. We note that URM status can be visually observable by peers and professors, while FG status is not. Our survey of student perceptions and attitudes found that agreement or disagreement generally matched for all four studied groups, meaning that if URM FG students on average agreed (or disagreed) with a statement, all the other groups matched that sentiment. This suggests no glaring or overt differences in experiences with the professor, classmates, or class. However, there was often a systematic trend in the strength of agreement or disagreement. For example, in Fig. 2I not-URM not-FG students strongly disagreed ($\bar{x} = 1.3$, standard deviation [SD] = 0.6) with the statement "My race affects the way my classmates think about me," while URM FG students mildly disagreed ($\bar{x} = 2.3$, SD = 1.1). This difference provides a clue into how URM and FG students experience and perceive the Biology 101 classroom.

In general, prompts related to perceptions and attitudes about the professor were similar for all groups studied. The only exception was the prompt "My race affects the way my professor thinks about me." (Fig. 2D). This indicates that URM FG students feel their professor thinks about them differently due to their race. Even a small difference in treatment (microaggressions) can lead to students devoting thought to whether they are being mistreated (29). This type of cognitive effort, debating whether the comment or action was racist and considering what action to take in response, is known to negatively impact learning and success in the classroom (49–52). Indeed, the more ambiguous the comment or action, the more challenging it is for the individual (51, 52).

Of note, this difference in student response did not appear in statements about the professor caring, taking their questions seriously, or comfort in seeking help from the professor (Fig. 2A to C). This suggests professors need to improve their self-awareness (53); it is also clear that professors can improve the general comfort students have in seeking outside help.

Additionally, since differential perceptions of classmates were more striking, how the professor facilitates classroom dynamics may be particularly important.

All prompts related to classmates and peers reveal a difference between URM FG, URM not-FG, and often, not-URM FG students compared to their not-URM not-FG counterparts. There is a clear concern about how URM and FG students feel they are perceived by their peers. A student's sense of belonging has been correlated with greater academic effort, greater likelihood of participating in class discussions, and positive emotional engagement (54, 55). Class belonging is more tightly linked to these behaviors than major belonging or university belonging (54), again suggesting the classroom as a crucial target for efforts to remove disparities in URM success in STEM. While professors cannot be there to monitor every interaction, they can set the tone for how peers and groups should behave (37). Instructor talk is any language not directly related to the classroom concepts (38). Instructor talk can help instructors mitigate the feeling of stereotype threat and establish the classroom culture to mitigate students utilizing cognitive energy to determine whether they are being negatively stereotyped or whether their performance is a reflection of their group (38, 52, 53, 55–57).

Future work

This work looks at the intersectionality of URM FG students. We would have liked to look at intersecting identities such as women of color or LGBTQIA + people of color (POC); however, our samples are much too small. We firmly believe studies centering on intersectionality in STEM are lacking in the current literature and are an important aspect needing emphasis. Similarly, we were unable to examine many possible confounding factors, such as whether URM students had greater burdens of work, family obligations, or other outside factors that might have affected their persistence and experiences. In order to increase the sample size for studies regarding intersectionality, as well as to see if our results can be replicated, we would like to collaborate with other small, liberal arts PWI institutions.

This research also revealed that our URM students felt less prepared for Biology 101 even at the beginning of the semester (Fig. S1). This feeling persisted throughout the course, and the difference was still present at the end of the semester. This area seems a good place to further investigate students' feelings about their level of preparedness and how it affects their mindset, anxiety, and performance during the course. Results from this avenue of research could provide insight into interventions that might have a positive effect on student outcomes. We would recommend that all interventions begin with faculty developing self-awareness and empathy, as described by Dewsbury and Brame (53) before focusing on students (58–61).

Other considerations

Though we believe our findings shed light on the experiences of URM students in Biology 101 courses, there were some limitations to consider. We could not compare pre- and post-

surveys; therefore, we were unable to draw direct conclusions about whether experiences in Biology 101 changed students' ideas about biology, STEM careers, or themselves. Counts of URM students in our sample were too small for us to conduct several useful analyses. We hope future research can collect data from a larger sample of students to investigate intragroup qualities and be more precise in handling URM student groups. Finally, while we attempted to remain alert to potential sources of bias in our research, all the researchers self-identify as white, and as a result our research reflects our social position as white people; additionally, we acknowledge that quantitative methods may themselves be biased in ways that we may not have detected (62).

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

SUPPLEMENTAL FILE 1, PDF file, 0.2 MB.

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We declare no conflicts of interest.

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