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Inspiring STEM undergraduates to Tackle the AMR Crisis

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22 Running Title: Inspiring STEM undergraduates to Tackle the AMR Crisis

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24 Key Words: Research-led teaching, Antimicrobial Resistance, STEM graduates,
25 Undergraduate Education

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27 One Sentence Summary: In addition to the traditional research-led lecture, different
28 teaching approaches using multiple modes of instruction can be used in a biology-
29 centric department to incorporate antimicrobial resistance as a topic into an
30 undergraduate curriculum.

31

32 Abstract

33 To address the growing problem of antimicrobial resistance (AMR) it is necessary to
34 invest in, inspire and attract future generations of scientists to this research area.
35 Undergraduate education should be a focus for attention and efforts should be
36 made to ensure that students are afforded opportunities to actively engage with
37 AMR. We illustrate how as a topic, AMR provides opportunities to deliver effective
38 research-led teaching in addition to traditional teaching methods. We have used a
39 selection of case studies to illustrate how students can be engaged with AMR using a
40 variety of research-led approaches to develop the required skills for biology-centric
41 students. In addition we indicate how these skills map to the UK Quality Assurance
42 Framework and the Vision and Change report developed by the American
43 Association for the Advancement of Science.

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50 **Introduction**

51 Recent media attention has raised public awareness towards the major societal
52 concern of antimicrobial resistance (AMR). Dame Sally Davies the Chief Medical
53 Officer in the UK (2011) referred to AMR as *'one of the greatest threats to modern*
54 *health'*. This growing awareness has led to many new reports, (Shallcross and Davies
55 2014)(Earnshaw *et al.* 2009)(President's Council of Advisors on Science and
56 Technology 2012) and funding streams and initiatives
57 (<http://www.mrc.ac.uk/research/initiatives/antimicrobial-resistance/>;
58 <http://www.niaid.nih.gov/topics/antimicrobialresistance/Pages/default.aspx>). The
59 televised Longitudinal prize award particularly caught the public imagination in the
60 UK, resulting in AMR being the focus of a £10 million research prize (
61 <https://longitudeprize.org/>) . Recently, this dire warning also attracted the attention
62 of the current UK Prime Minister, David Cameron. He called for a review to
63 investigate both the multifaceted problem of increasing AMR as well as the
64 diminishing investment in new antimicrobial discovery. A report (2015) has been
65 published as a direct output of this review: *'Tackling a global health crisis: the initial*
66 *steps'* (The Review on Antimicrobial Resistance 2015). It proposes a series of
67 interventions to stimulate antimicrobial development to be underpinned by
68 commercial activity. These initial proposals include a call to *'Invest in the people who*
69 *will solve the problem'* and that *'It is crucial to train the next generation of doctors,*
70 *scientists, microbiologists, pharmacologists, medicinal chemists and biochemists, as*
71 *well as economists, social scientists and vets, among others.'*

72

73 **The Role of STEM Graduates**

74 Tackling the international threat of AMR must involve the next generation of Science
75 Technology Engineering and Maths (STEM) graduates. In the UK this is reflected in
76 the Quality Assurance Agency benchmarks statements for Biosciences and
77 Biomedical Sciences taught in Higher Education. The subject benchmark statement
78 for Biosciences includes a paragraph specifically relating to antibiotics; *'the*
79 *biosciences have much to contribute to the health and wealth of the nation.*
80 *Fundamental understanding of diseases, for example, the role of microorganisms,*
81 *together with the development of [...] antibiotics, has saved many lives'* (Quality

82 Assurance Agency for Higher Education 2007a). Similarly the benchmark statement
83 for Biomedical Science degree draws attention to the major health risk of antibiotic
84 resistant bacteria (Quality Assurance Agency for Higher Education 2007b).

85 Modern society relies heavily on STEM and is dependent on STEM graduates to
86 address global problems such as AMR. Yet evidence suggests that fewer school-aged
87 children are choosing STEM subjects as a career path (Donghong and Shunke 2010)
88 even though the state-mandated National Curriculum was introduced to schools in
89 1989 to ensure that science was a core subject from the age of 5-16 years. This is a
90 concern as research by the UK Science Council suggests that in 2017 over 58% of
91 jobs will require skills in STEM subjects (The SCORE partnership 2011). However, this
92 recruitment problem is not restricted to school pupils. Recent reports have
93 highlighted a similar trend in undergraduate populations with students choosing not
94 to major in the sciences on both sides of the Atlantic in the UK and the USA.
95 Economic projections indicate that, in the US, there is a predicted shortfall of more
96 than 1 million new STEM graduates over the next decade (President’s Council of
97 Advisors on Science and Technology 2012). The Engage to Excel report (2012)
98 outlined issues with uninspiring undergraduate courses, difficulties with developing
99 maths skills and an unwelcoming atmosphere within faculties as factors that
100 encourage students to switch to non-STEM disciplines.

101

102 Tackling the growing problem of AMR will depend on the interest of future
103 generations of STEM graduates to provide solutions. Stimulating interest and
104 awareness of the complexity of this problem within an undergraduate curriculum is
105 desirable. Clearly, one way we can do this is to examine how we embed research
106 about AMR in university curricula.

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108 **The Role of Research-Led Teaching**

109 The importance of the links between research and teaching in undergraduate
110 education has been viewed as a priority for student education with a report by the
111 UK Department for Education and Skills in 2004 stating *“it is important to see this as*
112 *an issue about ensuring that research-informed teaching takes place in all HEIs”*. The

113 links between research and teaching have been debated and critiqued. Boyer *et al.*
114 (1997) examined the relationship between teaching and research in HEI curricula.
115 They also considered the benefits that a curriculum that combines research and
116 teaching can bring to students and faculty members of staff, while considering how
117 research and teaching can be embedded and facilitated. Griffiths (2004) followed by
118 Healey (2005) developed a Teaching-Research Nexus. It has two axes that highlight
119 the role of active student engagement in the process and differentiated between
120 understanding the physical processes involved with research as opposed to learning
121 about the results of research outputs. Within this nexus students experience four
122 relationships of Teaching-Research links in their subject-based departments. This
123 Teaching-Research Nexus can be considered in terms of AMR (Figure 1):

- 124 • Research-Based teaching with students as active participants, where students
125 are actively engaged as researchers and the teaching is designed around
126 inquiry-based activities. The division between teacher and student is
127 minimised. In science curricula, this has conventionally been delivered as the
128 final year research project, which can be focussed on projects assessing AMR
129 mechanisms or potential new antibiotic discoveries. (Case Study 1 and 4)
- 130 • Research-Orientated teaching where the student is a recipient of teaching.
131 The students learn about research processes that underpin new knowledge.
132 The division between teacher and student is apparent. In science curricula,
133 this learning has conventionally been delivered as laboratory practicals that
134 may use antibiotic resistance marker methodologies. This can also be
135 delivered in classes that develop critical analysis of the primary research
136 literature in the field of AMR. (Case Study 3 and 5)
- 137 • Research-Led teaching, in which the student is the passive recipient of
138 knowledge and information about research findings that can often be related
139 to the research interest of the staff delivering the teaching. The division
140 between teacher and student is apparent. In science curricula, this has
141 conventionally been delivered in a lecture format where lecturers have the
142 opportunity to inform students about the latest research in the field of
143 antibiotic discovery.

144 • Research-Tutored teaching involves the student as an active participant. In
145 science curricula this has conventionally been delivered in ‘Oxford style’
146 tutorials where students actively engage with tutors within discussions about
147 research findings and may produce papers or essays focussed on antibiotic
148 discovery. The division between teacher and student is minimised. (Case
149 Study 2)

150

151 Embedding research into biology undergraduate curricula was also addressed in The
152 Vision and Change in Undergraduate Biology Education report in 2009 (Bauerle *et al.*
153 2011). The report recommends the use of innovative pedagogy along with
154 integration of authentic research experiences and building key skills in mathematics
155 to encourage student engagement and retention in STEM. It uses case studies to
156 illustrate how to successfully embed enquiry-based teaching within undergraduate
157 programmes. Interestingly, the Engage to Excel report (President’s Council of
158 Advisors on Science and Technology 2012), also recommends replacing standard
159 laboratory courses with discovery based research courses to engage and excite
160 students with empirical research. Below, we also use case studies to illustrate how
161 different approaches using multiple modes of instruction can be used in biology-
162 centric departments, to incorporate AMR as a topic into an undergraduate
163 curriculum in addition to the Research-Led traditional lecture.

164

165 **In summary**

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167 The study of AMR can be incorporated into undergraduate biology-centric curricula
168 using a variety of various educational approaches that map to the Teaching-Research
169 Nexus and offer alternatives to the traditional lecture. These different approaches
170 have the potential to be adapted to different curricula and to attract the interest of
171 future generations of doctors, scientists, microbiologists, pharmacologists, medicinal
172 chemists and biochemists to provide solutions to this growing problem. We also
173 believe that other curricula including postgraduate curricula, which incorporate
174 different aspects of AMR may benefit from a similar scrutiny and mapping exercise.

175 Moreover, it is also important that the interest of potential STEM graduates towards
176 AMR is captured prior to University. Therefore we suggest that there is scope to use
177 aspects of these different approaches and modes of instruction illustrated in the
178 case studies to incorporate AMR teaching into schools.
179 (<http://www.sgm.ac.uk/outreach/small-world-initiative/>)

180

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260 **Table 1 Case Study 1:** Stakeholder perspectives in the Antimicrobial Resistance Crisis
261 (University of East Anglia)
262 *Research-Based Teaching*

263 Science undergraduates benefit from taking an issues-based approach to understand
264 how advances in science and technology concerning AMR impact upon society
265 (Bowater, 2013) (Bauerle et al., 2011). An effective way to introduce this to curricula
266 is via interactive, small-group teaching (Springer et al., 1999). A two-hour workshop
267 session allows students to explore the multifaceted problem of AMR. Firstly,
268 students are provided with a short, tutor-led introduction to revisits and reinforces
269 student's previous learning on antibiotic targets and AMR mechanisms. Next
270 students are introduced to the dual problem of increasing AMR and the diminishing
271 investment in new antibiotic discovery. The tutor actively encourages students to
272 produce a list of key stakeholders required to tackle these dual problems;
273 pharmaceutical companies, general practitioners, the agricultural industry, policy
274 makers and members of the public are often proposed. Students divide into small
275 groups that represent key stakeholders in order to answer:

- 276 • how and why their stake-holder contributes to this global crisis
- 277 • what steps could be taken to provide solutions to this global crisis from the
278 viewpoint of the stakeholder and society in general.

279 The tutor encourages students to undertake online research during the session to
280 find the information and evidence required to develop arguments. Students are
281 required to capture and share their group learning using short presentations to the
282 whole workshop group within the final plenary session. During the session student
283 engagement with this global issue was generated as evidence by the fact that all
284 students contributed to the discussion during the final plenary. In addition students
285 suggested initiatives to address AMR such as labelling food to indicate their possible
286 levels of antibiotics. After the session, students write a short report to reflect on
287 their own learning. Students were sufficiently interested to engage in further
288 research outwith the workshop as indicated in by their reflective reports that
289 provided evidenced of additional reference to the research literature surrounding
290 AMR. Student evaluation comments of the session included '*this was a particularly*
291 *interesting session, as it not only educated us on the issues but truly hit home as to*

292 *how difficult it is to come up with a solution giving us a proper understanding of this*
293 *issue.'*
294

295 **Table 2 Case Study 2:** Critical Analysis of AMR literature with a social media presence
296 (University of Strathclyde)
297 *Research-tutored teaching*
298 Final year undergraduates benefit from learning how to critically appraise the
299 literature, enabling them to develop skills and knowledge not only on research
300 outcomes but also how certain methodologies can be employed to answer a
301 research question (Quality Assurance Agency for Higher Education, 2007a)(Quality
302 Assurance Agency for Higher Education, 2007b)(Bauerle et al., 2011). One of the best
303 ways to facilitate this kind of learning is via student participation and cooperative
304 problem solving opportunities using a discussion based delivery (Knight and Wood,
305 2015). Active discussion between students can be encouraged and facilitated by the
306 tutor through the use of social media such as Twitter - active learning has been
307 shown to improve student learning outcomes (Knight and Wood, 2005) and
308 extending this conversation beyond the classroom
309 ([http://www.academiccommons.org/2014/07/21/teaching-with-twitter-extending-](http://www.academiccommons.org/2014/07/21/teaching-with-twitter-extending-the-conversation-beyond-the-classroom-walls/)
310 [the-conversation-beyond-the-classroom-walls/](http://www.academiccommons.org/2014/07/21/teaching-with-twitter-extending-the-conversation-beyond-the-classroom-walls/)).
311 Final year Microbiology students are firstly tutored in how to read and appraise a
312 scientific paper and to critically analyse the work. Next they are provided with a
313 selection of research papers and asked to choose a paper that interests them. The
314 'Twitter-handle' (Twitter name) of the author(s) is provided to the student(s) and the
315 authors are informed their paper is chosen. Papers are selected from the literature
316 by the tutor to reflect the breadth of work related to AMR, from molecular
317 mechanisms of both resistance and biosynthesis, antibiotic discovery, biotechnology
318 etc. All class papers are available to students, to encourage them to read widely,
319 followed by a period of student-centred learning where the class critically appraise
320 the papers they are studying. Students are also encouraged to 'tweet' the authors
321 with questions relating to their work. Tutors facilitate and stimulate discussion
322 amongst the class and with the authors of the papers and potentially the wider
323 scientific community through tweets and the use of class-specific #Hashtags. During
324 the class presentations (Journal club style) the class are encouraged to tweet about
325 their research on the papers, and through the use of #hashtags these can form a
326 useful resource to influence student revision. There is also potential to 'Storify'

327 (<https://storify.com>) with the class #hashtag to provide an automated summary of
328 all tweets containing that #hashtag and email or tweet this to the class. The
329 presentations normally last 20-30 minutes and have time for discussion following the
330 presentation. Students can be assessed on their presentation skills and critical
331 analysis skills. There is also the potential to use peer-marking approaches with this
332 format. Anecdotally, from our work students who engage with Twitter discussion
333 generally score higher marks on the class, but this likely reflects their overall level of
334 engagement in the subject. A more detailed trial of 125 students also showed a
335 correlation between Twitter use and grades (Junco et al., 2011). We found using this
336 approach as with a face-to-face discussion based delivery still encourages variable
337 engagement from students. In addition Twitter engagement from the paper authors
338 can also be variable. Suggesting papers from authors who you know will engage
339 through Twitter is a solution to this issue. However we also noticed that shy students
340 or students who are uncomfortable with sharing their Twitter handles with a tutor,
341 can be encouraged to set up a class-specific account for themselves thereby
342 facilitating greater inclusion in online discussions as oppose to face-to-face
343 discussion settings. As tutors we could clearly observe that students found the
344 discussions stimulating and it enable wider engagement - where students explain the
345 subject to the wider public following a question. Clearly the format of Twitter also
346 encourages students to be succinct and ask their questions in 140 characters.
347
348

349 **Table 3 Case Study 3:** Learning the skills of a scientist; Writing papers about AMR
350 University of Strathclyde
351 *Research-orientated teaching*

352 Students, while learning within a course often develop abstract and theoretical skills
353 within microbiology. However, there is a need to introduce greater problem-solving,
354 analytical skills and writing skills to undergraduate courses (Quality Assurance
355 Agency for Higher Education, 2007a)(Quality Assurance Agency for Higher Education,
356 2007b)(Bauerle et al., 2011). Traditional essay writing, whilst useful for the former,
357 often does not enable acquisition of the skills that a practicing scientist requires –
358 such as data analysis and paper writing (Coil et al., 2010). To develop these skills a
359 data analysis and paper writing assignment for undergraduate students was
360 constructed. The students are presented with a detailed scenario that describes how
361 ‘they’ are a scientist who has completed a series of experiments and sequenced a
362 gene responsible for AMR in a specific organism. The students are provided with
363 appropriate data, a DNA sequence (the gene of interest), a series of numerical data
364 (growth curves, qRT-PCR etc) and some *in vivo* data. The students are also provided
365 with the ‘Instructions for authors’ for a scientific journal, such as ‘Microbiology’
366 (<http://www.sgm.ac.uk/publications/journals/microbiology.cfm>), and a sample
367 paper from the journal, to enable them to see how a manuscript is put together for
368 that journal. They are asked to go and write the manuscript (with the exception of a
369 materials and methods section). This process requires the students to use a range of
370 skills they have learned during their degree – bioinformatics, statistics, data
371 visualization, literature searching, critical analysis etc. The students engage well with
372 the work, often describing it as ‘challenging but enjoyable’, and they generally
373 achieve good marks as they engage well with the assignment. Interestingly we
374 noticed that the way students approach the task reflects their own interests;
375 students with biochemistry interests often focus on the protein and align the
376 translated sequence, picking out active sites; immunology students often focus on
377 the interaction with the host; and microbiologists can focus on the AMR
378 mechanisms.

379 Overall the assessment is amenable to any subject and allows students to learn skills
380 that they can see will be useful to them as scientists. Moreover, by supplying

381 appropriate data, assessments of this kind allow students to develop the analytical
382 skills required to develop a deep understanding of AMR.
383

384 **Table 4 Case Study 4:** The Small World Initiative (originated in Yale University)

385 *Research-based teaching*

386 Student retention and engagement is more likely if students take part in authentic
387 research experiences at an early stage in STEM curricula (President’s Council of
388 Advisors on Science and Technology, 2012) (Bauerle et al., 2011). The Small World
389 Initiative (SWI), developed at the Center for Scientific Teaching at Yale, is designed as
390 an undergraduate research course where students are used to crowd source the
391 search for new antibiotics (<http://smallworldinitiative.org/about#about>). Initially
392 first year students’ culture soil microbes and screen for antibiotic activity against the
393 human pathogens that are currently causing concern because of their growing
394 resistance to Antimicrobials: the so called ESKAPE pathogens (*Enterococcus faecium*
395 [E], *Staphylococcus aureus* [S], *Klebsiella pneumoniae* [K], *Acinetobacter baumannii*
396 [A], *Pseudomonas aeruginosa* [P] and *Enterobacter* Sp. [E]; Boucher et al., 2009),
397 thus addressing a real-life problem. Using standard laboratory protocols, students
398 are encouraged to design their own experiments, analyse data and produce
399 presentations about their research project. Providing students with opportunities to
400 experience the excitement and process of research in the first years of Higher
401 Education in university and colleges provides a positive, realistic reflection of
402 science, resulting in higher retention rates within STEM fields. The SWI is currently
403 running at more than 59 diverse institutions across the United States (including state
404 universities, community colleges and non-traditional universities), United States
405 Territories and internationally within Puerto Rico, Belize, Malaysia and The United
406 Kingdom. Preliminary evaluation data based on pre and post SWI questionnaires and
407 course tests suggests that taking part in the SWI can increase undergraduate student
408 academic performance and encourage student engagement (Slone, 2015)(Caruso et
409 al., 2015). Currently the SWI is being adapted for used within School University
410 partnerships to encourage STEM participation in school pupils at a pre-university
411 stage. (<http://www.sgm.ac.uk/outreach/small-world-initiative/>)

412

413

414 **Table 5 Case Study 5:** Exploring Antibiotic action; a laboratory investigation

415 (Newcastle University)

416 *Research Orientated Teaching*

417 Developing effective laboratory skills is a key element of undergraduate Bioscience
418 and Biomedicine degree programmes (Quality Assurance Agency for Higher
419 Education, 2007a)(Quality Assurance Agency for Higher Education, 2007b) (Bauerle
420 et al., 2011). Embedding opportunities to develop confidence in mathematics is also
421 desirable (President’s Council of Advisors on Science and Technology, 2012). We
422 constructed a series of laboratory experiments focused on the action of β -lactam
423 antibiotics using the Gram-positive bacterium *Bacillus subtilis* as a model organism.
424 Three practical sessions were integrated into this experiment:

425

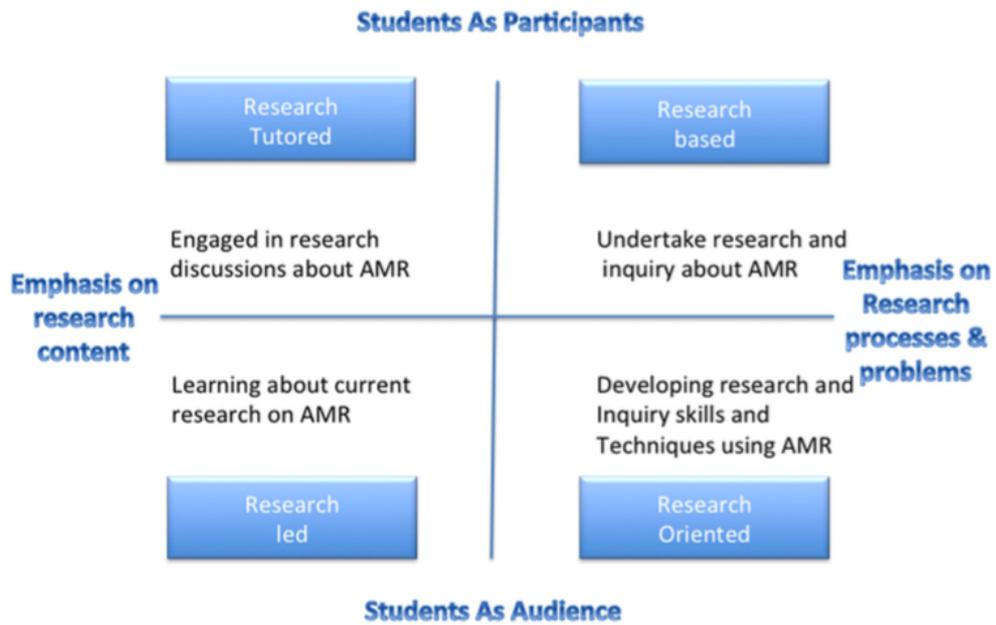
- 426 1. Bacterial sensitivity to antimicrobial compounds – using a disc diffusion
427 assays with eight antibiotics tested against six *B. subtilis* strains with or
428 without mutations in the genes encoding the penicillin binding proteins)
- 429 2. A Minimum Inhibitory Concentration (MIC) using microplate assays with one
430 antibiotic against the six *B. subtilis* strains from experiment 1.
- 431 3. Identification of β -lactam targets – Bocillin (Fluorescent Penicillin from
432 Invitrogen) is used in a competition assay with SDS-PAGE detection. Each
433 student challenges the six strains of bacteria with their antibiotic and then
434 Bocillin.

435

436 Students use the individual data sets to develop an understanding of how bacteria
437 react to antibiotics and to semi-quantitatively estimate the minimum number of
438 antibiotic molecules needed to kill a single cell. They also integrate the different
439 data sets into a written report. Students are supported throughout this process using
440 seminars focussing on the maths that underpin the data analysis of MIC calculations
441 and effective scientific report writing including the importance of self-editing their
442 own report writing. Students have shown that they are able to effectively integrate
443 three data sets in order to produce a scientific report. Students recognise that this
444 set of microbiology practical sessions allows them to develop practical microbiology
445 skills and a confidence in their maths and writing skills.

446

447 **Figure.1.** Represents the teaching nexus focused on AMR.



The research teaching nexus focused on Antimicrobial Resistance AMR. The teaching nexus is adapted from the Teaching Nexus with Permission from Professor Mick Healey

448