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Using design theory to foster innovative cross-disciplinary research: Lessons learned from a research network focused on antimicrobial use and animal microbes' resistance to antimicrobials

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ABSTRACT

Dealing with the major societal and research challenges related to antimicrobial use will require cross-disciplinary research and strong relationships between researchers and stakeholders. Design theories, such as the concept-knowledge (C-K) theory, can help spur the emergence of innovation. Here, our objective was to examine how the C-K theory could promote the development of novel, cross-disciplinary research projects on antimicrobial use and animal microbes' resistance to antimicrobials. A French research network (R2A2; Réseau Recherche Antibiotiques Animal) was created whose goal was to foster cross-disciplinary research and scientific discussion on these topics. The R2A2 network hosted general meetings and thematic workshops, during which participants brainstormed using C-K diagrams. The network's performance was evaluated through the evolution of C-K diagrams, project creation, and participant interviews. R2A2 led to the creation of a minimum of eight research projects. The participants felt network events facilitated interactions and collaborations with researchers in different disciplines. The R2A2 network has opened new avenues of research into several important topics: antimicrobial use on farms, the environmental impacts of antimicrobials, animal immunity, and alternative treatments. The keys to its success were: (i) participant interest; (ii) the use of C-K design theory to encourage cross-disciplinary thinking; (iii) the aim of fostering several small projects rather than one large project; and (iv) network responsiveness to participant needs with regards to meeting and workshop topics. C-K theory served a key role in promoting cross-disciplinary thinking on topics at the interface between research and stakeholder interests.

1. Introduction

1.1. The challenges involved in designing innovative research on antimicrobial use and microbes' resistance to antimicrobials in animals

Antimicrobial resistance is now one of the major challenges in human and animal health. Indeed, the intensive use of antimicrobials in farming systems (Chevance & Moulin, 2011) has led to resistance to antimicrobial in livestock (EFSA, 2006). In parallel, there has been an increase in resistance to antimicrobial in humans, which has raised questions regarding current veterinary and medical practices. Current levels of antimicrobial use in livestock have contributed to the poor image that consumers have of animal production chains. Only a few new antimicrobial compounds have been developed in the last 20 years, and there is no reason to expect this rate will increase in the near future (ECDC, 2009). Thus, existing antimicrobials must be carefully used to preserve their effectiveness against major bacterial diseases in animals and humans. A complementary and broader current concern in animal production is the desire to develop sustainable farming systems, which have fewer negative impacts on the environment and should become economically viable in the long term (Dumont, Fortun-Lamothe, Jouven, Thomas, & Tichit, 2013). Limiting the use of medicinal compounds, including antimicrobials, is one of the goals in sustainable farming systems.

Given this set of circumstances, antimicrobials need to be used sparingly and appropriately, and action must be taken to curb antimicrobial resistance. With these goals in mind, several different policies have been implemented in France, the EU, and other parts of the world.

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For instance, France's ECOANTIBIO program includes different measures for reducing antimicrobial use (Ecoantibio, 2012). However, if antimicrobials are restricted, farmers will need to have alternatives for preventing infectious diseases and increasing livestock resistance to diseases, all while preserving productivity. To be successful, such programs will require research-derived knowledge, farmer acceptance, and the use of alternative strategies at several organizational levels.

In this context, we created an INRA-funded research network (R2A2, Réseau Recherche Antibiotiques Animal) focused on antimicrobial use and microbes' resistance to antimicrobials in animals. Its objectives were (i) to encourage cross-disciplinary thinking by bringing together researchers and stakeholders from public and private sectors and (ii) to promote the development of research projects aiming to reduce antimicrobial use and the risk of antimicrobial resistance on farms. However, the building of the network was shrouded with many unknown and uncertainty on how to run it.

1.2. The challenge of cross-disciplinary innovation in research

The challenges posed by antimicrobial use and microbes' resistance involves a diversity of fields of study including microbiology, epidemiology, clinical medicine, nutrition, and genetics. Similarly, a more informed use of antimicrobials and alternative treatments could result from collaborations among pharmacologists, clinicians, epidemiologists, and microbiologists. These collaborations aim to develop innovative strategies that meet both the animal health objective of infectious disease control and the public health objective of limited effects on animal microbiota. The contributions of sociologists and economists could also be crucial in order to consider the perceptions and attitudes of farmers towards disease and to carry out a cost-benefit analysis focused on preventive measures and alternative treatments. However, since science is becoming more specialized, promoting innovative cross-disciplinary research proves to be challenging and often provides mixed results (Dewulf, François, Pahl-Wostl, & Taillieu, 2007; Karniouchina, Victorino, & Verma, 2006; Kostoff, 1999). Especially, several studies have shown that mobilizing knowledge from different disciplines does not always ensure the generation of new ideas. Indeed, thinking along discipline-specific lines helps to properly structure existing knowledge, but it does not provide new ways of representing or designing complex links among disciplines.

In order to build these new links, cognitive barriers have to be overcome during the design of new research programs: several studies have shown that, when seeking to building new innovative solutions, people tend to propose mostly common and unoriginal solutions (Agogué, Le Masson, & Robinson, 2012; Crilly, 2015; Jansson & Smith, 1991). This effect is called "fixation effect" (Jansson & Smith, 1991). For instance, when exploring original solutions so that an egg, which would be dropped from a 10-meter-high building, does not break, 80% of the solutions proposed belong to three classical categories: protecting the egg, slowing down the fall and damping the egg (Agogué et al., 2012). More original solutions may be reached, such as playing on the physical properties of the egg (e.g. boiling the egg and then freezing it to enhance its resistance to impact). Regarding antibiotic resistance, it could therefore be expected that researchers of R2A2 would have preferentially questioned the invention of new antimicrobials and experience difficulties exploring new categories of solutions, especially solutions relying on new links between disciplines. Fixation effects therefore could have shut doors to innovative, possibly essential, ways of approaching the given challenges regarding resistance to antimicrobials in animals.

To help avoiding fixation, enhancing the cross-disciplinary nature of the propositions could be a first strategy: in practice, when relationships among disciplines are scarce, design mainly leads to monodisciplinary projects. Such projects can be innovative but only within their realm of study. Disciplines can be combined in sequential order, where knowledge from different disciplines is contributed progressively. This interdisciplinary approach is typical for engineering or development projects. For instance, to improve a vaccine, a researcher could first work on the virus' virology and then address host immunology. Finally, disciplines can also be combined in networks. In such transdisciplinary scenario is likely to foster innovative ideas because it forces to link new knowledge bases, which were not previously related, and to deal with new ways of seeing the design issue (Le Masson, Hatchuel, & Weil, 2016). However, being able to control the cross-disciplinary nature of the design exploration, as well as controlling the defixation process, was neither intuitive nor easy for R2A2 leader and members.

Innovative design methodologies have been developed and implemented in order to overcome fixation effects. Among them, the KCP process helps enhancing both cognitive and organizational aspects of the defixation process (Le Masson, Hatchuel, & Weil, 2009). The KCP approach relies on the C-K theory (Hatchuel & Weil, 2003, 2009), which offers a theoretical framework to model and enhance the design process and also helps visualizing the knowledge bases that are mobilized to develop new design paths. Such logic could help rationalizing and controlling the design process followed during R2A2 meetings, ensure defixation and help controlling of the cross-disciplinary nature of the concepts addressed.

Given the challenge raised by the creation of the R2A2 network, the leader of the network therefore called on design theory experts to help emerging novel cross-disciplinary ideas thanks to the KCP and C-K methods. The objective of the paper is to present the design approach developed in order to foster innovating research on antimicrobials in the context of the R2A2 network. We explain how we organized the approach, what were the outputs and evaluate the added value to the design approach. The following section first details the specificities of the R2A2 network. It then presents the KCP process and the C-K theory logics and explain how they were mobilized to organize the R2A2 activities and ensure the design of new innovative projects.

2. Materials and methods

2.1. R2A2 network management and meetings

The R2A2 network was led by one senior researcher in animal epidemiology (C. Ducrot). It was headed by a steering committee (a group of 5 people from various origins) that finalized the meeting agendas. This agenda was beforehand discussed with a group dedicated to the implementation of the design approach, called the "C-K group" and composed of 3 design experts (researchers in innovative design), the R2A2 leader, and a small number of volunteer expert biologists. The agenda also took into consideration the ideas and interests raised during previous meetings, the schedule and content of new project calls. An average of three meetings was held per year.

Each meeting was divided in two parts: in the first part talks were given by researchers or practitioners in order to introduce knowledge or new results regarding a selected topic. The second part consisted in small workshops addressing specific issues that had been identified. The CK group discussed the questions to be brought up during meetings, the ways to overcome questions of interest for which no project or leader were clearly identified and proposed specific design workshops based on specific CK discussions.

From 2013 to 2016, 10 one-day meetings were organized. On average, 39 people attended each meeting. The disciplinary breakdown was as follows (mean number of people): 23.4 researchers, 5.7 veterinarians or people from related fields, 5.4 representatives from technical institutes or the Ministry of Agriculture, and 4.5 representatives from the pharmaceutical industry. The researchers came from a wide range of disciplines, from molecular biology to the human-focused sciences, such as microbiology, animal production, nutrition, clinical medicine, pharmacology, epidemiology, and sociology. Overall, 133 different people attended at least one meeting, among which 69 (52%)

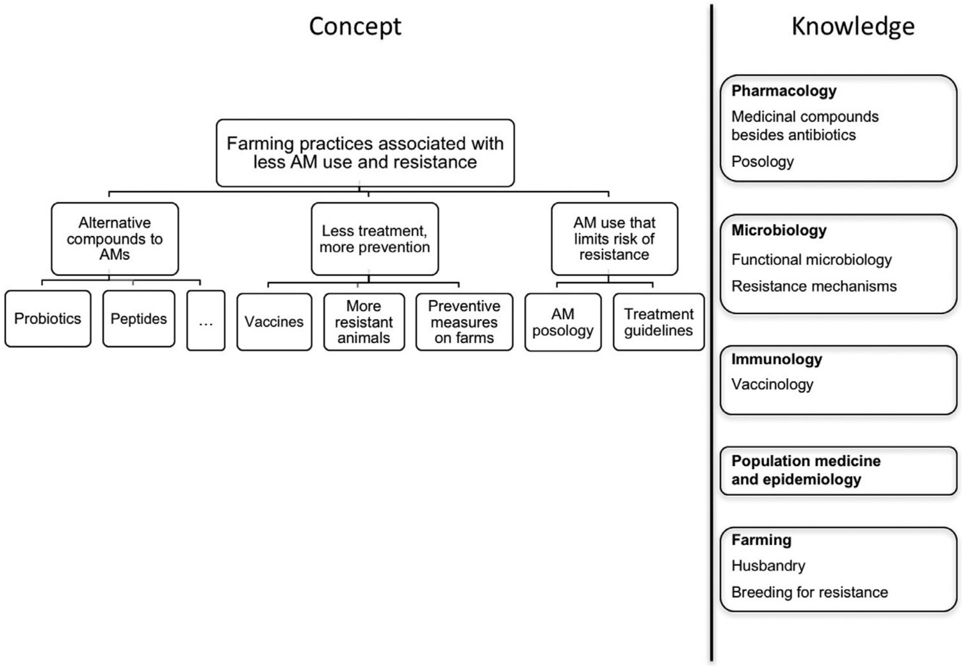

Fig. 1. Representation of the first concept-knowledge diagram (C-K1). The concept space (C-space) contains propositions without a logical status: it is impossible to prove that they are either true or false. The knowledge space (K-space) contains propositions with a logical status, known to be either true or false. Innovation emerges through a co-expansion of both C-space and K-space. AM: antimicrobials; (…) refers to other possibilities.

attended more than one meeting.

2.2. C-K theory and KCP process

The concept-knowledge (C-K) theory (Hatchuel & Weil, 2003, 2009) seeks to understand the reasonings according to which innovation occurs. It also helps exploring new innovative design paths according a specific logic: C-K models the interaction between the knowledge space (K) and the concepts space (C), which corresponds to new unknown ideas (Fig. 1). The K-space harbors propositions with a logical status: they are either true or false. The C-space contains propositions without a logical status: it is impossible to prove that these statements are either true or false in the knowledge space. For instance, if we have certain common-knowledge definitions of a chair or a boat, a “footless chair” or a “flying boat” could be examples of concepts. Concepts are often composed of known properties found in K-space, which, when combined, constitute an unknown object. Moreover, the C-space is relative to the K-space: concepts are defined based on a specific base of knowledge. For example, if one thinks about a cushion, the “footless chair” then becomes knowledge. Hatchuel and Weil (2009) explained that innovation and disruptive ideas emerge from the dialogue between the C-space and the K-space. Innovation also emerges through a co-expansion of both the C- and K-spaces. When an original concept arises, it constitutes an “expansive partition.” In practice, original concepts are the result of surprising knowledge and are sometimes quite distant from the initial concept. Regarding design activities related to scientific research, modeling this interaction between K and C is particularly interesting: while research often focus on knowledge expansion, design in research plays on this strong interplay between the discovery of new knowledge and the generation of new concepts (new products, new experimentations or new research projects).

Because C-K theory only addresses the cognitive aspects of design, the KCP process has been developed to address both the cognitive and the organizational aspects of innovation (Elmquist & Segrestin, 2009; Le Masson *et al.*, 2009). Based on C-K theory, the KCP process presents four steps: (1) the initialization phase, (2) the K-phase, (3) the C-phase, and (4) the P-phase. Relying on an initial C-K mapping related to the exploration of the design issue, the initialization phase organizes the contents of the K and C phases, where the K-phase consists in sharing knowledge related to the design issue – both recently developed knowledge directly addressing the issue and disruptive knowledge belonging to other innovation fields – and the C-phase consists in concept generation sessions, which explore specific sub-topics. Finally, the P-phase helps transforming original concepts that were generated during the C-phase, into projects that are led according to the institution rules (for instance, regarding project funding, project development or even publication)

2.3. Application of C-K and KCP approaches to R2A2 activities

Initialization - In order to identify existing representations in the topic of antimicrobial resistance in farms and to identify innovative research questions, an initial C-K tree was built and then improved by the R2A2 scientists with the assistance of C-K experts (C-K1). This first C-K diagram was then discussed and improved within the C-K group. Altogether three general C-K diagrams were drawn to map the general exploration of the network and identify topics to be discussed in meetings.

K-, C- and P-phases within the R2A2 meetings - At the beginning of the network, the meetings were organized to foster cross-knowledge between participants. Thus, general topics such as microbial use in the different farming systems were addressed. The associated workshops aimed to work on projects that had been identified at the start of the project and were not necessarily associated with the morning presentation. After one year of network, the aim of the network was more targeted at exploring new innovative paths. Therefore, some of the meetings were more built as KCP workshops: presentations in lines with interesting missing knowledge were held in the morning and concept generation workshops were organized in the afternoon. The P-step was mostly led between the meetings by R2A2 steering committee with project leaders identified during the R2A2 meetings.

2.4. The approach evaluation

Evaluating the value of the design approach used by the network was difficult because no standard of reference is available. Usually, evaluation procedures employ criteria such as publication probability. The difficulty here was that the network's output is full of interdependent links. Consequently, we evaluated network performance via three means: the comparison between the first C-K diagram (C-K1) and

Table 1
V2OR evaluation criteria.

	Variety	Value	Originality	Robustness
C-K diagrams	Balanced ratio between height and width; well-distributed concept paths	Identification of potentially valuable elements	Large number of expansive C and K partitions	Resistance of concepts to changes in context
Projects	Involves multiple disciplines	Includes novel stakeholders	Reveals benefits of the metaprogram structure	Has a wide range of applications

third C-K diagram (C-K3), the different research projects that were established and participant interviews. The criteria we used to do this qualitative evaluation were based on criteria of the V2OR method (Agogué, Hooge, Arnoux, & Brown, 2014; Le Masson, Hatchuel, & Weil, 2007). This method employs a set of four evaluation criteria that are adapted to concept generation: variety, value, originality, and robustness (Table 1). It was applied by the design specialists and was based on qualitative criteria.

- Concept variety is obtained by avoiding the proliferation of too many similar ideas. The variety criterion was used to determine whether the network focused on a single topic or explored diverse subjects and how it reflected the cross-disciplinary nature of the network.
- Exploration value refers to the identification of potentially valuable elements: for example, it could be useful to generate new knowledge regarding stakeholders (e.g., suppliers, customers, and third parties) and their tastes or expectations. The value criterion was used to reveal how much value the network's activities added in the form of research projects (e.g., via the involvement of new stakeholders, identification of new applications).
- Concept originality refers to the emergence of surprising properties and the renewal of objects' identity. This was employed to assess the novel benefits that the projects yielded and the network's cross-disciplinary nature.
- Exploration robustness is the most complex of the criteria. In rule-based design, robustness refers to object feasibility (e.g., technical, legal, commercial, or societal). For innovative designs, new robustness criteria may have to be identified depending on the concept paths taken. Robustness thus more generally refers to the reliability of concept paths, which can be assessed by determining concept resistance to changes in context and by the quality and quantity of knowledge associated with the concept. The robustness criterion served to verify that the set of research projects could have broad applications.

Participant interviews were conducted to investigate whether the network had helped participants acquire new contacts and generate novel ideas. They did not take place at the beginning but after the R2A2 network had worked for 3-4 years. Indeed, leading interviews at the beginning of the project may influence participant behavior and opinion regarding the process (McCambridge, Witton, & Elbourne, 2014). The interviews were qualitative in nature and targeted seven different participants' profiles (i.e., project leaders, workshop leaders, field veterinarians, industry workers, researchers, representatives from government agencies, and representatives from technical institutes). The interviews were conducted by the same person (a C-K expert). Each interview lasted between 45 min and one hour and a half. During the interviews, participants were asked to express their general opinion about R2A2 and any suggestions on how it could be improved. They also addressed interactions among disciplines, meeting organization, how the participant's opinions on antimicrobial use and resistance may have changed, whether opportunities for project funding had resulted, and how knowledge gained during meetings had been applied.

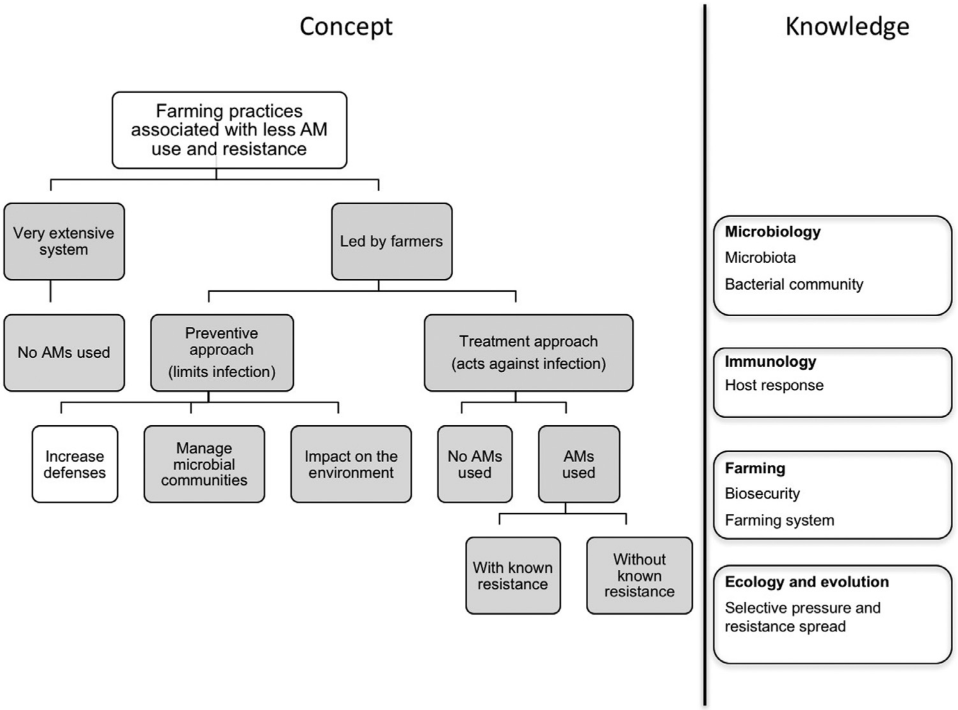

Fig. 2. Representation of the second concept-knowledge diagram (C-K2) (only the initial partitions are shown). The main differences in the concept space with Fig. 1 are indicated in light gray. AM: antimicrobials.

3. Results

3.1. Outputs of the KCP initialization: the C-K diagrams

The KCP approach started by mapping the research concept and the knowledge mobilized at the beginning of the network activity. The first C-K diagram (C-K1, Fig. 1) that was generated by the researchers in biology, without C-K experts. It resulted in a diagram structured along disciplinary lines. It presented a list of possible solutions with very few links between disciplines. For example, there was a distinction between pharmacological research focused on compounds other than antimicrobials and research in microbiology, population medicine, and pharmacology focused on antimicrobials and microbiological mechanisms.

Meeting frequency was quite high the first year [5] to create a sense of belonging among network participants and to encourage people to get to know each other better. They were dedicated to bring basic disciplinary knowledge to participants, such as knowledge regarding curative approaches.

The C-K1 was worked with the help of C-K experts. In order to create linked between disciplines they proposed to explicit action undertaken by farmers. For instance, to use alternative compounds, one must first diagnose the problem and/or diagnose the disease, select the animals to treat, and then treat them. This opened new pathways management of microbial communities and exploring the unknown area of treatment by AM without resistance. New knowledge had to be mobilized, such as microbiota, ecology and evolution. The diagram brought in different disciplines in a sequential order (Fig. 2). The associated meetings dealt with new logics such as preventive approaches.

The next step was to dedicated to test the robustness of the diagram and to open new unexplored paths. To test the robustness of the diagram, we checked with the group that we had not forgotten any major conceptual level in the C-K tree. This was the case with the detection step, which was thus added (early / routinely detection). The final diagram (C-K3, Fig. 3) end up mobilizing knowledge regarding sociology and economics, engineering sciences and targeted treatment. It involved more varied stakeholders and disciplines than the first C-K diagram. Then, the C-K group identified the disruptive paths that could allow presenting interesting knowledge during R2A2 meetings (K-phase) and lead to the generation of original concepts by the R2A2 members (C-phase). At this point (the last two years), the following meetings were all dedicated to identified knowledge and concepts of interest for R2A2 meetings (such as microbiota and health, therapeutic alternatives to antibiotics, social sciences applied to the use of antimicrobials). New people and disciplines were progressively targeted (microbiology, nutrition, social sciences) and involved in the network. Twenty-one workshops were held over the same time period (Table 3).

3.2. Outputs of the K, C and P-phases: workshops topics and project generation

At least nine projects emerged directly from the first workshops (Table 2); they each had a clear leader and encompassed several disciplines. However, some workshops did not lead to any projects, even though interesting ideas had been put forward. When this occurred, we contacted researchers working on the topic and invited them to chair a working group; we helped them organize a series of follow-up workshops to dig deeper into the issue of interest. These workshops were of longer duration and occurred in tandem with the regular meetings. This approach was used to address four major topics that were rather complex: (i) farmers' failure to comply with biosecurity measures and practice good hygiene (three workshops); (ii) the way in which farmers handle the problem of metaphylaxis (i.e., treating a large group of animals when only some are diseased; four workshops); (iii) identifying antimicrobials that do not impact the microbiota (three workshops); and (iv) the spread of antimicrobial resistance in farms and the environment (seven workshops).

Different levels of success were associated with these four thematic clusters, illustrating that various pathways can be used to tackle such complicated research questions. An example of a clear success was the metaphylaxis cluster. Following the workshops, participants very quickly designed, submitted, and received funding for a cross-disciplinary project focused on optimizing the metaphylactic use of antimicrobials in poultry (OMAP). The discussion that took place during the

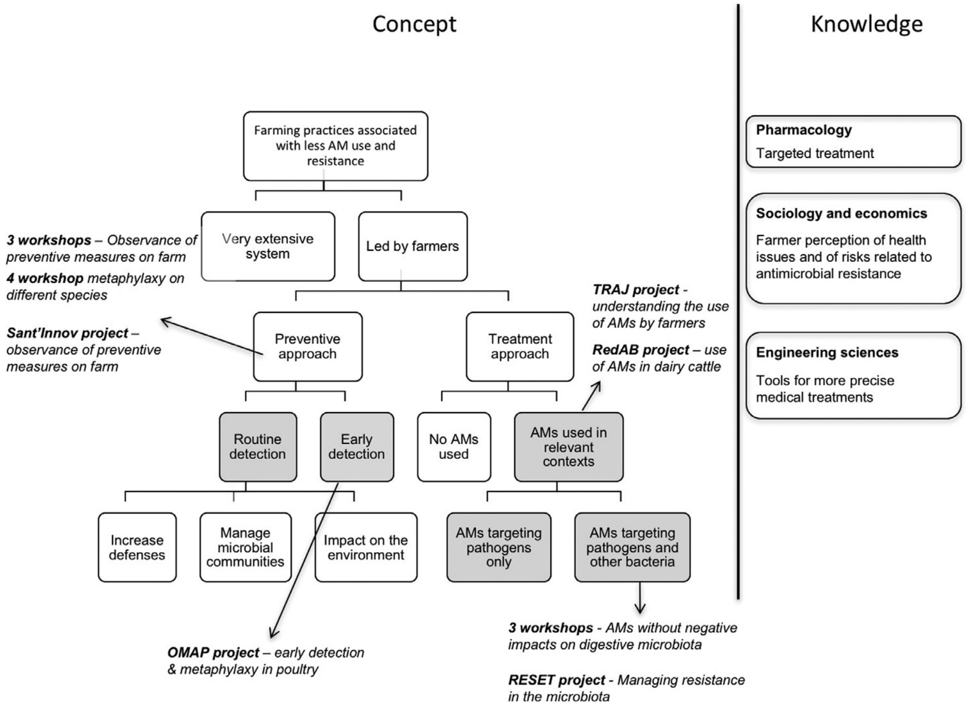

Fig. 3. Representation of the third concept-knowledge diagram (C-K3) (only the initial partitions are shown). The main differences in the concept space with Fig. 2 are indicated in light gray. The main projects that were built in relation to the C-K diagram are indicated in italic. AM: antimicrobials.

workshop lead to innovative research topics, and the appropriate experts were represented during workshop discussions. Furthermore, a relevant call for proposals came out at around the same time, which motivated the researchers to prepare a submission. Their project aims to identify the social and technical factors that drive change in the metaphylactic use of antimicrobials in poultry. The first facet seeks to identify the issues that influence antimicrobial use by poultry farmers and is exploiting sociological and epidemiological approaches. The second facet is focused on developing a new and more efficient system for the early detection of disease symptoms on poultry farms; it draws on knowledge from the fields of epidemiology and clinical veterinary medicine as well as field observations. The third facet aims to optimize the dosing of antimicrobials in drinking water using more accurate estimates of daily water consumption by poultry and pharmacological modeling. It builds on knowledge in the fields of pharmacology and modeling and includes an experiment in an experimental facility.

The cluster addressing the spread of antimicrobial resistance in farms and the environment was a more mitigated success. We initially lacked the appropriate expertise in the research network. It could have been probably expected but not easy to forecast. As a result, the first two workshops were inconclusive. In 2015, we took advantage of the early announcement of a European call for proposals on this topic to organize a meeting dedicated to this theme. We expanded the expertise found in the network by sending invitations to several researchers who study human health, controlling antimicrobial resistance in hospital settings, the evolution of antimicrobial resistance in manure and manure fermenters, and models of the spread of antimicrobial resistance. Various talks were given to bring participants up to date in these research domains, and three workshops were held in tandem and focused on different scales (i.e., genes and cells, animals and humans, and food chains and the environment). Various research questions were developed, and there was networking among researchers from different fields. The workshops did not immediately produce testable research questions. The main reason seems to be the lack of cheap and easy-to-use tools that allow the detection of resistance genes in various types of biological samples. However, the relationships established among the researchers were fruitful because researchers finally submitted at least three collaborative projects (ANTIBIOSUD 2014, AntibioReComBa 2014, and ECARGAHIT 2014, cf Table 2).

It was more difficult to quantify the results of the cluster focused on farmer compliance with biosecurity and use of good hygiene practices. Different ideas did emerge from the workshops, and they ended up being included in larger research projects and extensions of pre-existing projects, which were already in preparation when the network meetings were being held. One of these projects was focused on the social factors involved in changing antimicrobial use on poultry farms, and another was looking at innovative approaches for reducing antimicrobial use on dairy cattle, beef cattle, and pig farms. Furthermore, other diverse ideas emerged from the workshops and were included in other projects. Overall, it has been difficult to quantify how the network contributed to the number of proposals submitted.

Finally, in the case of the cluster addressing the development of antimicrobials that do not impact the microbiota, interesting ideas emerged but sufficient expertise was lacking. Furthermore, the representatives from the pharmaceutical industry could not speak freely on all topics. Some ideas were related to issues outside of competitive concerns and could therefore have been discussed openly in the presence of representatives from different companies. Others, in contrast, were the basis for industrial competition, and an open cross-disciplinary discussion was not the proper way to promote collaborative research involving pharmaceutical companies. To be handled productively, this topic would require a different approach.

The varying success of these different clusters illustrates that each topic involved different and sometimes contrasting components requiring alternative pathways for promoting innovation and project building. Furthermore, it underscores that scientific, economic, and social factors play a key role in the successful establishment of cross-disciplinary research projects. Consequently, if a KCP approach is applied, the organization of the conceptive work, the input of knowledge and work on concepts will need to adapt to the context such as the possibilities to mobilize researchers and other actors, the scientific and organizational barriers, the pre-existing links and fixation. Thus, the success of applying the design theory relies on very flexible and adaptive attitude.

3.3. *Evaluation*

3.3.1. *Analysis of C-K diagrams*

The first diagram (C-K1, Fig. 1) was of low value and presented little originality: it included no new stakeholders except for farmers and was structured along disciplinary lines. Indeed, the first partition was discipline based. The last diagram (C-K3), however, displayed a high degree of variety and originality (for example, with regards to the concept of early detection). Value was also added by the inclusion of new stakeholders, such as veterinarians, laboratories, farmers, technicians, suppliers, and environmental agencies. Robustness could be further enhanced by the acquisition of missing knowledge, which could help develop the expansive partitions identified.

3.3.2. *Analysis of R2A2 projects*

We found that the set of research projects emerging from the network's efforts demonstrated a high level of variety: diverse concepts were put to use and different paths to innovation were followed. Variety also manifested itself in the cross-disciplinary nature of the projects, which brought in diverse fields such as sociology, microbiology, epidemiology, nutrition, pharmacology, and the veterinary sciences. Each project displayed a different mixture of disciplines.

Exchanges among seemingly disparate disciplines can also enhance the originality of any resulting research projects. For instance, the TRAJ project (Table 2) shows that sociology, the animal sciences, and the

Table 2
Projects that emerged from the R2A2 network (through the end of 2016).

Acronym	Name	# Teams	Disciplines involved	Funding status
TRAJ	Trajectories of change in antimicrobial use in livestock production	12	sociology, animal sciences, veterinary medicine	funded
AntibioReComBa	Spreading of resistance to antimicrobials along the food chain	3-4	microbiology, epidemiology, pharmacology	submitted
RESET	Use of microbiota from healthy animals for disease prevention	4	microbiology, nutrition, pharmacology	funded
ECARGAHIT	Method for tagging resistance genes in bacterial strains [the purpose was to further develop studies on the spread of resistance]	5	microbiology, nutrition, pharmacology	submitted but rejected
ANTIBIOSUD	Ecology and transmission of antibiotic-resistant bacteria in humans and animals in Burkina Faso and Vietnam	8	microbiology, molecular epidemiology, modeling, applied medicine	submitted but rejected
RedAB	Reducing the use of antimicrobials in dairy cattle	5	sociology, animal sciences, veterinary medicine	funded
SANT'Innov	Innovating on farms to balance ecology and competitiveness: an animal health perspective	9	sociology, economics, animal sciences, veterinary medicine, microbiology	funded
OMAP	Optimizing metaphylactic use of antimicrobials in poultry	5	sociology, epidemiology, pharmacology, clinical medicine, modeling	funded

Table 3
List of R2A2 workshops.

Date	Subject of workshop
10/04/13	Understanding farmer attitudes using sociology
10/04/13	Management of antimicrobial resistance
10/04/13	The spread of antimicrobial resistance in the environment
13/06/13	Antimicrobials without negative impacts on digestive microbiota
13/06/13	The spread of antimicrobial resistance in the environment
04/10/13	Antimicrobials without negative impacts on digestive microbiota
04/10/13	Prevention of infectious diseases on farms
13/12/13	Antimicrobials without negative impacts on digestive microbiota
13/12/13	The spread of antimicrobial resistance in the environment
21/03/14	Boosting the resistance of animals to microbes
21/03/14	Understanding farmer non-compliance with preventive measures
19/06/14	Metaphylaxis—alert thresholds
19/06/14	Metaphylaxis—targeting animals for treatment
29/11/14	Metaphylaxis in pig farming
29/11/14	Understanding farmer application of preventive measures
01/06/15	Appropriate protective commensal flora in animals
01/06/15	Metaphylaxis in poultry farming
01/06/15	Understanding farmer application of preventive measures
18/11/15	Antimicrobial resistance—genes and cells
18/11/15	Antimicrobial resistance—animals and humans
18/11/15	Antimicrobial resistance—food chains and the environment

veterinary sciences can be successfully combined. More specifically, it addresses the trajectories farmers could take to decrease antimicrobial use by employing very different perspectives: i) sociological considerations, such as personal beliefs and social ties with veterinarians and farming organizations and ii) animal-related concerns stemming from the animal and veterinary sciences, such as prevention and monitoring efforts. The results of the sociological research were interpreted with the help of experts in the field of poultry farming. The project could have gone even further and yielded more complete findings by addressing economics and farm management.

With regards to value, the different projects were valuable because they included new stakeholders, such as veterinarians, farmers, and representatives from the pharmaceutical industry. Furthermore, they had value within the research community itself, given the large number of research teams that become involved, as well as the funding that was obtained. A major success of the R2A2 network has been that it has brought together experts with different backgrounds together to build projects. For example, veterinarians worked with agricultural scientists and thus became strongly engaged in promoting sustainable farming through the mutual goal of decreased antimicrobial inputs. Starting with applied questions and daily observations of farmers and farming activity, researchers were able to formulate important diverse scientific questions that were then addressed thanks to a cross-disciplinary collaboration. If we take the project on metaphylaxis in poultry as an example, we can see that three different questions were addressed by clinical veterinarians, sociologists, epidemiologists, and pharmacologists.

Finally, the robustness of the network's performance was very difficult to evaluate because it meant determining whether the different projects were resistant to potential changes in context, such as a change in study species, bacterium, or antimicrobial compound. Given the network's current stage of development, it is likely that introducing new knowledge (e.g., identifying resistance genes in the environment) or shifting the study context (e.g., working on very different species, such as fishes) would modify network outcomes. That said, the network's output to date would remain relevant.

3.3.3. Results of the participant interviews

The interviews highlighted the network's role in promoting knowledge acquisition, idea development, project elaboration, and professional contacts. The participants were satisfied with the network's responsiveness, as illustrated by its ability to adapt its program to address important topics that were raised during the meetings and workshops. The network did not remain influenced by its initial knowledge-framed structure (i.e., along disciplinary lines). In terms of final suggestions, the researchers wished for more information regarding C-K design theory and the way R2A2 leaders mobilized it because they perceived the interest of the approach. The industry representatives were interested in having more of their colleagues participate, and the government officials would have been satisfied with just receiving a summary of the workshops and did not feel the need to actually participate.

4. Discussion

We presented how the C-K design theory and KCP process were mobilized to foster the development of innovative cross-disciplinary projects related to important societal and research challenges associated with antimicrobial use in animals. The R2A2 network, which combined thematic meetings with targeted workshops to develop specific topics of interest, was organized according to the KCP methodology, which strongly relies on C-K theory. Altogether, these efforts led to the creation of at least eight stand-alone research projects; they also resulted in contributions to projects in development. The network was viewed as a resource that participants could use to collaborate and interact with people from other disciplines and sectors as opposed to a tool that was just focused on facilitating connections or funding. Here, we will focus on identifying what is the influence of the C-K design approach on the R2A2 network success, on what we consider have been the key factors in the network's success, the network's impact on the field of antimicrobial research, and the step difference between the KCP approach applied to an industrial context vs. in research.

4.1. Relationship between C-K design and R2A2 success

In this study, we showed that the R2A2 network has successfully evolved in term of generating ideas and creating cross-disciplinary projects. The causal relationship between the C-K approach and the R2A2 success is however hard to demonstrate because no reference standard is available. Nevertheless, several points highlight how R2A2 evolved with C-K design approach. First, we learnt from the comparison of C-K1 and C-K3. Indeed, C-K1, which followed disciplinary lines, could be viewed as the project structure without design effort. It is likely that cross-disciplinary thinking and problem-solving approaches would not have been encouraged. Reaching C-K3, we showed that the network was able to mobilize new knowledge and establish novel paths to innovation. Second, the R2A2 project stimulated a panel of 9 cross-disciplinary projects (that were or were not funded) that encompassed several disciplines. Third, the interviews highlighted participant opinion that the network moved away from their initial knowledge-framed structure and promoted knowledge acquisition, idea development, and project elaboration. This result was surprising because studies carried out in the private sector have shown that networks among firms are strongly influenced by knowledge regimes, especially if all the firms involved follow the same regime (Ozman, 2006). The R2A2 network managed to avoid this problem, and its participants thought outside disciplinary lines. Through the interviews, the participants expressed that the principles of C-K design theory could have been explained more explicitly, which would have allowed participants to have a better view of the network's overarching strategy.

Thus, altogether, we can conclude that introducing design effort fosters idea generation, cross-disciplinary links and projects. However, we did not demonstrate that the C-K approach is the only way to achieve this goal. Because C-K theory seeks to organize the design around complex heterogeneous domains rather than the discipline, our effort moves towards a trans-disciplinary approach rather than a multi-disciplinary approach that tends to juxtapose disciplines. However, the balance between the different kind of cross-disciplinary approaches is hard to evaluate.

4.2. Key factors behind the success of the R2A2 network

R2A2 benefited from a boost associated with its focal subject: indeed, the issue of antimicrobial use and resistance to antimicrobials in animals attracts today strong interest from researchers, industrial partners and practitioners (farmers and veterinarians). Furthermore, INRA gave the network funding, visibility, and legitimacy via its metaprogram on the integrated management of animal health. However, as this study has shown, R2A2 has lived up to its potential. Its participants viewed it as a resource for helping projects to emerge and supporting cross-disciplinary interactions. These factors led to the network's success for three main reasons.

First, using C-K design theory, participants acquired an overview and a “road map” of the different subjects and research topics related to antimicrobial use in animals. The way in which the C-K diagrams changed over time revealed that a more cross-disciplinary approach was emerging, which essentially resulted from the adoption of an alternative mode of partitioning (i.e., knowledge crossing). The first diagram was largely structured along disciplinary lines. For instance, there was a distinction between pharmacological research focused on compounds other than antimicrobials and research in microbiology, population medicine, and pharmacology focused on antimicrobials and microbiological mechanisms. The second diagram was framed by existing sequential links between disciplines. However, the third diagram created new links among disciplines. Using C-K design theory, participants identified new conceptual models, which is a mark of success for cross-disciplinary research (Stokols, 2006). Changes to the diagrams largely resulted when participants were asked to consider the actions that needed to be taken, to incorporate new knowledge to bolster ideas, and to question why some ideas were not developed. Indeed, the topics highlighted over the course of the R2A2 meetings and workshops are quite different from those included in the ECOANTIBIO plan. In the research section of the plan, topics are presented in a very compartmentalized way (Ecoantibio, 2012) (e.g., immunity and vaccines, new antimicrobial molecules, reduced antimicrobial use, impact of antimicrobial use on the environment) and sociological research is completely absent. To facilitate cross-disciplinary interactions and promote the use of C-K theory, we had participants work in a small group that combined scientific researchers and design theory experts. Although more time was invested to help everyone master the use of C-K theory, segregation along disciplinary lines was avoided.

Second, our methodology favored the emergence of numerous smaller projects as opposed to one large project. This approach has the advantage of drawing in a broader cross-section of people, because they can take on different roles in different projects. Three main drivers were behind the successful emergence of projects: i) the efficiency of the brainstorming process during workshops, which more or less led to innovative and testable research topics; ii) the appropriateness of the group's combined expertise; and iii) the existence of a call for proposals to motivate the participants. Although research projects can draw on several disciplines, it helps when it is framed around a core discipline to ensure that a clear project leader can be identified and that the project can be submitted to a specific funding program. This methodology can be very successful, as seen in the example of the poultry metaphylaxis project. This cross-disciplinary project contained three research axes and was rapidly funded. However, this success was not repeated for all the themes addressed.

Third, although the network's focus (antimicrobial use and resistance) and organizational structure (thematic meetings and workshops) always remained the same, the network adapted over time to respond to the participants' needs. Initially, meetings were frequent (every few months the first year), short (lasting one day), and easily accessible (in Paris). Furthermore, a written summary of what occurred at the meeting was available to those who were absent. Also, participation in the network was open, meaning that new people could register at any time. Changes were made to meeting and workshop planning based on the output of the previous meetings and workshops and the results of the C-K diagrams. We made sure that all the topics of interest identified in the diagrams were addressed.

4.3. The network's impact on the field of antimicrobial research

The greatest impact derived from the R2A2 network was that links were established between fundamental research and applied questions, which resulted from interactions among disciplines and between scientists and non-scientists. When discussion shifted towards fundamental research, the network participants focused on analyzing the types of basic research that might be important in helping to solve applied questions and that could thus yield practical outcomes. An example is the study of the mechanisms underlying antimicrobial resistance. Delving into this topic could lead to the production of rapid tests that can detect resistance in field samples. It could also enhance our understanding of how and why antimicrobial resistance is spreading in the environment, which could help identify ways of controlling this problem at the animal or farm level.

4.4. Concept-knowledge design theory in research versus industry

This study applied an innovative design theory and method in a context where people are particularly influenced by their initial knowledge regimes: the scientific disciplines. In the past, C-K design theory has been successfully applied in industry settings (Hatchuel, Le Masson, & Weil, 2004), where participants are often strongly influenced by the knowledge regime of their organization. Most of the time, this regime corresponds to knowledge about the composition of material goods (Ozman, 2006). In methodologies aiming for innovative design, participants are indeed often stymied by the base and structure of their initial knowledge, which can negatively impact creativity (Abraham & Windmann, 2007; Agogué et al., 2014; Hatchuel, Le Masson, & Weil, 2011; Le Masson et al., 2011). In the R2A2 network, it was challenging to help participants avoid thinking along disciplinary lines, which likely would have led to monodisciplinary concepts. To promote the emergence of original concepts, the fixation on a discipline-based structure had to be avoided. The changes across time in the C-K diagrams show that such a fixation was overcome. Moreover, the fact that the network was able to adapt the research topics and meeting/workshop organization to participant needs shows that the knowledge base and structure mobilized by the network were continually changing.

5. Conclusions

The increasing number of complex research topics that involve the veterinary sciences means there is a need for highly cross-disciplinary approaches (Rosenfield, 1992; Stokols et al., 2003) and strong relationships between researchers and stakeholders. There is also a real demand for innovative research that truly expands the boundaries of what is known and that can respond to existing needs. These requisites are also now being applied by an increasing number of funding agencies and programs (e.g., ANR, H2020) (Bromham, Dinnage, & Hua, 2016; Lyall, Bruce, Marsden, & Meagher, 2013). Here, we addressed these needs by establishing a network that employed C-K design theory to foster discussion on antimicrobial use and resistance to antimicrobials in animals; the ultimate goal of generating research projects was successful. The C-K diagram is an important tool that can help encourage cross-disciplinary thinking on applied research questions raised by stakeholders and can promote disciplinary decompartmentalization by favoring cross-disciplinary approaches. Such research networks need to be structured to take into account both individual interests (e.g., researchers are interested in building knowledge) and collective interests when seeking to come up with innovative research questions. Network efficacy is based on the ability to bring together individuals with appropriate expertise, frame testable research questions, and time discussions to correspond with calls for proposals. The R2A2 network was effective in (i) raising important applied questions on the improved use of antimicrobials on farms and the impact of antimicrobial treatments on the environment and (ii) building cross-disciplinary research projects addressing these two topics.

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Competing interests

The authors declare that they have no competing interests.

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