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Abstract: The fostering of interdisciplinarity is increasingly requested of research organizations. However, conventional approaches to academic research management limit our understanding of the way interdisciplinary research (IDR) centers integrate multiple disciplines. This paper proposes a multilevel approach to explore the patterns of knowledge integration and the forms of research organization emerging from the practices and activities of IDR centers. Several bibliometric-based, network-oriented and visualization-rich approaches are used. The cases of two prominent IDR centers are considered: Harvard University's Wyss Institute and Kyoto University's WPI-iCeMS. At the macro level, our results show similarities in the scientific positioning of both IDR centers, which translate into differences in the nature, intensity and drivers of their knowledge interconnections at the meso-level. At the micro-level, we demonstrate that far from idealizations of full convergence, the realities of IDR centers are characterized by heterogeneous patchworks of multi-trajectory research domains-some of these enabling, others generating interdisciplinary knowledge. Differences in knowledge integration occur between but also, and more importantly, within IDR centers. Thus, tailored strategies tuned to the particularities of organizations and topic-based forms of research organization appear to cope better with interdisciplinary knowledge. The understanding of these inter- and intra-organizational differences proves crucial for effectively fostering knowledge integration. An integrated model relating levels of research management and visualization approaches is proposed for the management and assessment of knowledge integration in IDR centers.

Multilevel exploration of the realities of interdisciplinary research centers for the management of knowledge integration

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Highlights

- A multilevel approach macro, meso, and micro levels is proposed for the exploration of interdisciplinary research (IDR) centers.
- We study the patterns of knowledge integration and the forms of research organization emerging in the practices of IDR centers in Japan and the US.
- Our results demonstrate that the realities of knowledge integration in IDR centers are far from their typical idealizations of full convergence.
- We provide cues about the management, organization, and assessment of knowledge integration in IDR centers.
- An integrated and systematic understanding of knowledge integration proves crucial for fostering interdisciplinarity.

Graphical abstract



Multilevel exploration of the realities of interdisciplinary research centers for the management of knowledge integration

The fostering of interdisciplinarity is increasingly requested of research organizations. However, conventional approaches to academic research management limit our understanding of the way interdisciplinary research (IDR) centers integrate multiple disciplines. This paper proposes a multilevel approach to explore the patterns of knowledge integration and the forms of research organization emerging from the practices and activities of IDR centers. Several bibliometric-based, network-oriented and visualization-rich approaches are used. The cases of two prominent IDR centers are considered: Harvard University's Wyss Institute and Kyoto University's WPI-iCeMS. At the macro level, our results show similarities in the scientific positioning of both IDR centers, which translate into differences in the nature, intensity and drivers of their knowledge interconnections at the meso-level. At the micro-level, we demonstrate that far from idealizations of full convergence, the realities of IDR centers are characterized by heterogeneous patchworks of multi-trajectory research domains—some of these enabling, others generating interdisciplinary knowledge. Differences in knowledge integration occur between but also, and more importantly, within IDR centers. Thus, tailored strategies tuned to the particularities of organizations and topic-based forms of research organization appear to cope better with interdisciplinary knowledge. The understanding of these inter- and intra-organizational differences proves crucial for effectively fostering knowledge integration. An integrated model relating levels of research management and visualization approaches is proposed for the management and assessment of knowledge integration in IDR centers.

1. Introduction

It is widely recognized that the production of knowledge and the various institutions involved in the science system are constantly transforming (Hessels and Van Lente, 2008). These changes are largely due to the increasingly complex scientific, technical, and societal problems facing research institutions (Anzai et al., 2012; Siedlok and Hibbert, 2014). Novel conceptions of and solutions to these challenges are believed to more likely arise from integrative or synthetic approaches cutting across multiple and disparate disciplines (NRC, 2014; Repko, 2008; Stehr and Weingart, 2000). Several labels are used to describe this phenomenon, such as "interdisciplinarity", "transdisciplinarity", "fusion", "convergence", "hybridization", "cross-disciplinarity", "anti-disciplinarity", and "cross-fertilization", among others (Battard, 2012; Islam and Miyazaki, 2010; Lauto and Sengoku, 2015; Moss, 2011). Despite their differences, these terms all imply the significance of the integration of different strands of expertise, theories, methods, or data (Repko, 2008; Wagner et al., 2011). To emphasize this common ground, the remainder of this paper uses the terms "knowledge integration" and "interdisciplinarity" interchangeably.

Knowledge integration is believed to lead to new knowledge (Huutoniemi et al., 2010). It has also been regarded as a potential source of competitive advantage and innovation (Siedlok and Hibbert, 2014; Siedlok et al., 2015). Several authors have expressed caution and skepticism about the promises of interdisciplinary approaches (Frodeman, 2011; Jacobs, 2013). Nevertheless, the increased interest in knowledge integration has led to its continuing and accelerating support in science and technology policy programs throughout the world (Anzai et al., 2012). New modes of production of integrative knowledge have emerged through the creation of research centers, programs, and courses with explicitly interdisciplinary aims (Hessels and Van Lente, 2008; Siedlok and Hibbert, 2014). These activities have embraced multiple fields of science and technology. Interdisciplinarity has been particularly influential on the life sciences (Burggren et al., 2010). Building on advances in molecular and cellular biology and genomics, interdisciplinary, high-impact life sciences research is expected to lead to innovative solutions and sustainable new technologies (Sharp and Langer, 2011). Recent reports have proposed the *convergence* of life sciences with physical, mathematical, computational, engineering, and social sciences as a way to accelerate innovation (MIT, 2016; NRC, 2014). Examples of convergent, interdisciplinary initiatives in the US include the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, the Precision Medicine Initiative, and the National Cancer Moonshot Initiative (MIT, 2016).

Over the years, numerous research efforts have been undertaken to elucidate the determinants (Siedlok and Hibbert, 2014; Stokols et al., 2008; Su, 2014; Van Rijnsoever and Hessels, 2011), processes (Lee et al., 2015; Siedlok et al., 2015), outcomes (Anzai et al., 2012; Bishop et al., 2014; Gowanlock and Gazan, 2013; Jensen and Lutkouskaya, 2014), or combinations of these aspects (Wooten et al., 2014) of interdisciplinary research. Other studies have approached interdisciplinarity more theoretically, such as in definitions of typologies (Huutoniemi et al., 2010; Siedlok and Hibbert, 2014), or more practically, such as in studies of its barriers and facilitators (Aldrich, 2014; CFIR, 2005; NRC, 2014). Although no consensus on the definition of "interdisciplinarity" has yet been established, all these studies have clarified its characteristic features: its scientific domain-dependence (Sanz Menéndez et al., 2001; Van Rijnsoever and Hessels, 2011), the coexistence of multiple forms of interdisciplinarity (Huutoniemi et al., 2010; Klein, 2008; Siedlok and Hibbert, 2014), its close complementarity with disciplinary knowledge (Jacobs, 2013; Stehr and Weingart, 2000), and its cognitive and social duality (Klein, 2008; Wagner et al., 2011). As knowledge accumulates, the need becomes urgent for research stakeholders to facilitate and foster interdisciplinary research in their organizations. Despite these calls, we know little about how interdisciplinary research centers integrate multiple disciplines in practice. It is hypothesized that knowledge integration in IDR centers is likely influenced by the features of interdisciplinarity mentioned above. However, no empirical research has yet demonstrated pragmatically how these features translate into the patterns of integration emerging from the practices and activities of IDR centers. Several assessment and measurement approaches have been proposed for this purpose (Anzai et al., 2012; Bishop et al., 2014; Gowanlock and Gazan, 2013; Jensen and Lutkouskaya, 2014; Kaplan et al., 2014; Rafols, 2014), but they have not been able to properly address the multi-dimensionalities, complexities, multiple levels of aggregation and granularity, and different perspectives inherent in interdisciplinary research (Cambrosio et al., 2006; Klein, 2008; Rafols et al., 2012; Rafols and Meyer, 2010; Sanz Menéndez et al., 2001). There is thus a clear need for empirical approaches to study the practices of knowledge integration in interdisciplinary research centers in a holistic, integrated, and multilevel manner.

Within this context, this paper addresses the following research questions: What patterns of knowledge integration emerge from the practices and activities of IDR centers?, and how do these patterns relate to their forms of research organization? To answer these questions, this paper uses the empirical cases of two convergent, life sciences-oriented research centers explicitly established with interdisciplinary aims: Kyoto University's Institute for Integrated Cell-Material Sciences (WPI-iCeMS) in Japan and Harvard University's Wyss Institute for Biologically-inspired Engineering (Wyss Institute) in the US. A three-level (macro, meso, and micro) analytical framework is proposed. Each level comprises a series of research activities that visually and quantitatively capture, from different degrees of granularity and perspectives, the cognitive structures underpinning research centers. For that purpose, this paper uses several bibliometric-based, network-oriented and visualization-rich approaches, including research landscape maps, science overlays (Leydesdorff and Rafols, 2009), density maps (Van Eck and Waltman, 2011), cluster mapping approaches, and heatmaps. The properties and dynamics of these cognitive structures are used as proxies for the patterns of knowledge integration and the forms of organization emerging in the practices of IDR centers. Knowledge integration is measured through the analysis of published scientific papers. The limitations of this method will be discussed in subsequent sections. Our results demonstrate that the realities of knowledge integration in IDR centers are far from their typical idealizations of full convergence. The similar scientific positionings of both IDR centers at the macro level translate into differences in the nature, intensity and drivers of their knowledge interconnections at the meso-level. At the micro level, IDR centers are characterized by heterogeneous patchworks of multi-trajectory research domains-some of these indirectly enabling, others directly generating interdisciplinary knowledge to different degrees. We argue that the exploration of the inter- and intra-organizational differences of IDR centers proves crucial for effectively fostering knowledge integration. An integrated model relating the levels of research management and visualization approaches is proposed for the management and assessment of knowledge integration in IDR centers.

The rest of this paper is structured as follows. Section 2 provides an overview of the relevant literature highlighting interdisciplinary research and approaches for its assessment in research centers. Section 3

continues with a description of the analytical framework and the case studies of this paper. Section 4 enumerates the data and research methods used. In Section 5, we report the findings of this study. Section 6 lists some of the main implications drawn from the study. Finally, Section 7 briefly concludes the paper.

2. Relevant literature

We first describe interdisciplinary research and knowledge integration, followed by a discussion of the roles of research centers established with explicitly interdisciplinary aims. This section finalizes with a review of studies assessing IDR centers, with a focus on studies using bibliometric approaches.

2.1. Interdisciplinary knowledge and research centers

The dynamics of science and technology are closely related to the generation, testing, and modification of knowledge (Loasby, 2002). Studies have described the evolution of knowledge as highly cumulative and path-dependent, featuring uncertain, open-ended, collective, and dynamically uneven processes (Consoli and Ramlogan, 2008; Nelson, 2003). The advancement of knowledge can take several routes; of these, knowledge that cuts across multiple and disparate disciplines has recently increased in importance (NRC, 2014; Repko, 2008). Such interdisciplinary knowledge is believed to be a potential source of competitive and innovative advantage (Huutoniemi et al., 2010; Siedlok and Hibbert, 2014; Siedlok et al., 2015), yet some researchers are skeptic (Frodeman, 2011; Jacobs, 2013). They plead for the dynamism, breadth, openness, and flexibility of disciplines, away from their prevailing view as isolated "silos" in the interdisciplinary studies literature (Jacobs, 2013; Repko, 2008).

Interdisciplinary research involves converging "data, techniques, tools, perspectives, concepts, and/or theories from two or more disciplines or bodies..." (CFIR, 2005). Integration is a defining characteristic of interdisciplinary research (Repko, 2008). It involves the (re-)combination of knowledge from disciplines, interdisciplines, and schools of thought through processes of knowledge transfer and creation (Repko, 2008; Siedlok and Hibbert, 2014). Knowledge integration has typically been characterized by its diversity (i.e. the disparity, variety, and (im)balance of given bodies of knowledge) and its coherence (i.e., the degree of interconnection between these bodies of knowledge) (Porter et al., 2007; Rafols, 2014).

There is still no clear consensus on the definition of "interdisciplinarity" (Wagner et al., 2011). However, a series of characteristics are repeatedly reported in the literature. Due to the intense context-dependence and multi-dimensionality of interdisciplinarity, we should expect multiple "interdisciplinarities" to coexist (Huutoniemi et al., 2010; Klein, 2008). This has led to explorations of the different modes of conducting interdisciplinary research through definitions of typologies and taxonomies (Huutoniemi et al., 2010; Siedlok and Hibbert, 2014). Other studies have examined the differences in interdisciplinarity across scientific research contexts (Frodeman, 2011; Sanz Menéndez et al., 2001; Van Rijnsoever and Hessels, 2011). Most have associated interdisciplinary research with application-oriented and problem-solving research (Van Rijnsoever and Hessels, 2011). For Heimeriks (2013), co-evolutionary processes among research, science, and society play a crucial role in these field-dependent differences of interdisciplinarity. Another important characteristic of interdisciplinarity is its high complementarity with disciplinary domains. This implies that both disciplines and interdisciplines are parallel, mutually reinforcing research strategies (Jacobs, 2013; Repko, 2008; Siedlok and Hibbert, 2014; Stehr and Weingart, 2000). Finally, the literature has described the cognitive and social duality of interdisciplinary research (Klein, 2008; Wagner et al., 2011). For Klein (2008), intellectual integration is tightly coupled socially through learning and other joint activities. Certainly, these features should impact the way interdisciplinary research centers integrate multiple disciplines. Nevertheless, we argue that there is still a need to pragmatically assess how these characteristics translate into the patterns of knowledge integration emerging from the practices and activities of interdisciplinary research centers.

Research centers are key vehicles for the convergence of scientists from multiple scientific backgrounds and the advancement of integrated scientific and technical knowledge (Battard, 2012; Bishop et al., 2014; Youtie et al., 2006). Research centers with explicitly interdisciplinary aims are regarded as a new kind of institutional innovation in the science system (Su, 2014). Interdisciplinary research centers provide both the internal

organization frameworks and the external interfaces that support knowledge integration (Anzai et al., 2012; Bozeman and Boardman, 2003). Their existence traces back to the early 1980's with the establishment of the "multipurpose, multidiscipline university research centers" in the US (Bozeman and Boardman, 2003). Recent examples include research centers moving into the convergence of the life sciences with mathematical, physical, engineering, and even social sciences (MIT, 2016; NRC, 2014). Over the years, the diffusion of interdisciplinary research centers has advanced through different trajectories (Thorp and Goldstein, 2013): (a) the creation of research centers housing scholars from disparate disciplines; (b) the organization of research centers focusing on emerging knowledge domains; (c) the creation of new departments or hybrid disciplines; and (d) the establishment of research structures with fundamentally different organizational principles. Interdisciplinary research centers encompass organizational, institutional, geographical, social, and cognitive dimensions, among others (Boschma, 2005; Rafols, 2014; Stokols et al., 2008). As these dimensions and their interplay can provide information for fostering and facilitating interdisciplinary knowledge, numerous assessment approaches have been proposed in the literature. The next section describes some of these assessment approaches, particularly those focusing on research centers and using of bibliometric approaches.

2.2. Assessment of interdisciplinarity in research centers and the role of bibliometric approaches

Over the years, research centers have been forced to find alternative approaches to demonstrate their success in achieving their missions. The research has highlighted that decision makers have tended to rely excessively on intuitive judgments (Porter, 2007; Porter and Newman, 2011). Hence, there is an urgent need to incorporate a richer base of empirical information into R&D management processes (Porter, 2007). Interdisciplinary research centers are not an exception, particularly since their assessment is still misunderstood (Bishop et al., 2014; Klein, 2008) and heavily dependent on the qualitative judgment of peer review (Anzai et al., 2012). This area of research is still in development. The assessment of interdisciplinary research still faces several hurdles (Anzai et al., 2012): (a) a lack of methodologies for the evaluation of research institutions, (b) the need to develop practical measuring for quantitatively and objectively measure interdisciplinary and collaboration, and (c) the need for methods of evaluating the effect of managerial approaches in organizations.

Numerous research efforts have attempted to assess interdisciplinary research centers. Some approaches have been restricted to the delineation of guidelines for the systemic evaluation of interdisciplinary research (Strang and McLeish, 2015). Others have focused on the assessment of transdisciplinary teams through researcher surveys (Mâsse et al., 2008) or mixed methods encompassing outcome-based, process, and developmental evaluations (Wooten et al., 2014). Bishop et al. (2014) corroborated the positive impact of interdisciplinarity on the productivity and collaboration of faculty affiliated with an interdisciplinary research center in the fields of mathematical and biological sciences. Focusing on the case of nanotechnologies, Battard (2012) proposed the "technological hub" concept to describe how scientists use multidisciplinary knowledge to create new scientific outcomes. Similarly, using the case of a nanotechnology research center, Kaplan et al. (2014) examined the challenges of multidisciplinary teams and organizations involved in the research on and commercialization of a nano-enabled biomedical device. Other studies have provided more qualitative descriptions of the barriers to and facilitators of interdisciplinarity in research centers (Aldrich, 2014; CFIR, 2005; NRC, 2014).

Many other studies have used tech-mining and bibliometric-based approaches to assess interdisciplinarity (Wagner et al., 2011). Anzai et al. (2012) measured the impact of interdisciplinarity on two large academic research projects in Japan. They proposed a series of key performance indicators (KPIs) for the measurement of the strategic fitness academic research projects on the basis of their interdisciplinarity and collaboration. Others have used bibliometric techniques combined with machine learning algorithms to assess the interdisciplinarity of an astrobiology research center (Gowanlock and Gazan, 2013), as well as its patterns of collaboration through social network approaches (Taşkın and Aydinoglu, 2015). Jensen and Lutkouskaya (2014) proposed a set of six quantitative indicators to measure the interdisciplinarity of 600 CNRS laboratories in France. These indicators are mainly based on typical numerical indicators used in interdisciplinary research studies, such as balance, variety, disparity, and diversity. At the researcher level, Pei and Porter (2011) assessed the research efforts of 21 leading nanobiomedical scientists on the basis of

interdisciplinarity and collaboration. These and other studies have relied on the science overlay approach developed by Leydesdorff and Rafols (2009) and Rafols et al. (2010), and later enhanced by Rafols (2014).

Thus, despite the numerous studies examining interdisciplinary research centers, few studies, if any, have attempted to explore interdisciplinarity from more integrated, holistic perspectives. Despite their drawbacks and limitations, which will be mentioned later, we believe that bibliometric mapping approaches are useful tools for the practical and systematic assessment of interdisciplinary research as they enable (a) the study of knowledge interactions from different perspectives (Shiffrin and Börner, 2004); (b) the use of bibliometric maps as powerful metaphors shaping the way we view, organize and classify the world (Milojević et al., 2012); (c) the revelation of structures from patterns visualized in the data (Fekete et al., 2008); and (d) the possibility for new knowledge to emerge from their visualizations (Heymann and LeGrand, 2014). The following section describes the analytical framework underlying such an approach.

3. Analytical framework and case studies

3.1. Analytical framework

The core of this paper is the integrated and multilevel framework shown in Fig. 1. The analytical activities underpinning Fig. 1 are based on a series of bibliometric-oriented, network-based, and visually-intensive approaches. These will be described in detail in the sections below.

[Figure 1 here]

Previous research has highlighted the benefits of a multilevel systems perspective for the study of scientific teamwork (Börner et al., 2010). Fig. 1 makes use of such an approach for the study of team science. In the analytical framework shown in Fig. 1, each of the three levels of analysis (macro, meso, and micro) approaches interdisciplinarity/knowledge integration from different perspectives and granularities:

- (a) Macro level: This activity locates research centers within their landscape of comparable organizations on the basis of their scientific knowledge bases. This "scientific positioning" relies on the construction of scientific research landscape maps.
- (b) Meso level: This activity characterizes and operationalizes the bodies of knowledge underpinning a given research center. In using the "science overlay maps" approach (Leydesdorff and Rafols, 2009; Rafols et al., 2010), the meso level aims to position these scientific knowledge bases within the whole of science. By doing so, it is possible to estimate the knowledge diversity and interconnectivity of research centers.
- (c) Micro level: At deeper levels of analysis, this activity seeks to explore the dynamics, structure and contents of the cognitive networks underlying the scientific production of research centers. In contrast to the previous activities, this level of analysis evaluates knowledge integration at the level of specific research topics.

As complex organizations, IDR centers can be dissected into the geographical, organizational, institutional, social, and cognitive layers that determine their behavior and performance (Battard, 2012; Boschma, 2005; Rafols, 2014; Stokols et al., 2008). Each of these layers provide the driving forces for the formation of networks, be it between countries or regions, organizational arrangements, institutions, people, or knowledge, respectively (Boschma, 2005). The analytical framework of Fig. 1 is mostly cognitive in nature as it relies on the production of scientific knowledge in IDR centers. As shown in Fig.1, the cognitive structures emerging from IDR centers are assessed from multiple levels of granularity and understanding. Depending on the level of analysis, these are regarded as scientific research landscapes, science overlays, or cognitive maps. In this paper, the dynamics, structure and contents of these cognitive structures are used as proxies for exploring the patterns of knowledge integration are likely influenced by the characteristic features of interdisciplinarity described in Section 2.1: scientific context-specificity, co-existence of multiple forms of interdisciplinarity, complementarity between disciplinary and interdisciplinary knowledge, and its cognitive-social duality.

The layers do not operate in isolation but interact with each other (Boschma, 2005). In fact, relating these dimensions allows an understanding of the dynamics of scientific research (Rafols, 2014). Accordingly, this paper relates the patterns of knowledge integration observed from the cognitive structures mentioned above to the forms of research organization in IDR centers. Both aspects provide crucial cues about the management and organization of their knowledge integration efforts. As shown later, the analytical framework of Fig. 1 will prove to be a practical and systematic approach for the understanding and assessment of the context and effects of managerial approaches in interdisciplinary research organizations.

3.2. Case studies

The empirical analysis of this study examines two leading-edge, interdisciplinarity-dedicated research organizations: the Institute for Integrated Cell-Material Sciences (WPI-iCeMS) at Kyoto University in Japan and the Wyss Institute for Biologically-inspired Engineering at Harvard University in the US. Both research centers are regarded as archetypes of organizations established exclusively to advance interdisciplinary research. Table 1 provides a general comparison of these research centers. They are fairly similar in terms of size and general fields of research. The rest of this section provides more detailed information on these research centers.

[Table 1 here]

3.2.1. WPI-iCeMS

The WPI-iCeMS (http://www.icems.kyoto-u.ac.jp/en/) was established in 2007 as part of the World Premier International Research Center Initiative (WPI), a high-end funding program led by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) in Japan. The WPI initiative strives to build "globally visible" research centers in Japan with four basic objectives: the advancement of leading-edge research, the creation of interdisciplinary domains, the establishment of international research environments, and the reformation of research organizations. As part of Japan's Third Science and Technology Basic Plan, the WPI initiative allocates selected institutes 0.5 to 2 billion yen per year (over US\$ 4 to 16 million) for a period of 10 years with the possibility of a five year-extension. The WPI-iCeMS seeks to create a new field of integrated cell-material sciences through the fusion of chemistry, physics, and cell biology. Two main knowledge-integrative approaches are derived from these interactions: materials for cell control and cell-inspired materials; the former refers to the creation of compounds to control processes in cells and the latter to the harnessing of the cellular processes to create chemical materials. Both approaches are supported by the understanding of synthetic methods and cellular processes and mechanisms.

3.2.2. Wyss Institute

The Wyss Institute (http://wyss.harvard.edu/) was founded in 2009 at Harvard University with a US\$125 million donation, doubled to US\$250 million in 2013, from Swiss entrepreneur Hansjörg Wyss. The Wyss Institute's mission is to "uncover nature's design principles and harness these insights to create new bio-inspired materials and devices that will revolutionize health care and create a more sustainable world" (Ingber, 2011). The Wyss Institute's innovation model is centered on disruptive change targeting early-stage scientific research as well as its translation and commercialization into marketable products. This dual stress on science and technology has resulted in the development of a novel research model for approaching science (Ingber, 2011, 2013). The Wyss Institute's focus on biologically-inspired engineering takes place along three main trajectories of interaction based on the understanding of nature's design principles: the development of bio-inspired engineering approaches, materials and devices, and applications in living systems, environment, and construction.

4. Data and research methods

For this study, the publications of both research centers were harvested from Thomson Reuters' database Web of Science (WoS). This study is restricted to articles and conference proceedings (except for the methods of Section 4.1.1), as it is believed that they are associated with scientific advances more directly than are review

articles and editorial materials. Additionally, only those publications coauthored by the principal investigators (PIs) or adjunct faculty members are assessed. The collected documents total 1,067 and 716 for the WPI-iCeMS and the Wyss Institute, respectively. These scientific publications underwent the series of bibliometric mapping approaches described below.

4.1. Bibliometric mapping approaches

The construction of the bibliometric maps of this study follows the general methods described in Cobo et al. (2011) and the references therein. This section describes the specific methods we used to construct the mapping approaches of the different levels of the conceptual framework shown in Fig. 1. High resolution images of the mapping approaches of this section are found at: https://sites.google.com/site/technovation2016idrmapping/.

4.1.1. Macro level of analysis: Scientific research landscape maps

The macro level of analysis relies on the construction of scientific research landscape maps. This mapping approach uses undirected two-mode networks (i.e. networks with two different types of nodes), relating research institutions (mode-1) with their respective fields of scientific research (mode-2). Following the literature, the scientific disciplines of research centers are approximated by the journal subject categories (SC) allocated to the total of their scholarly articles. SCs refer to the categorization scheme used by the WoS database to classify the scientific content of their journals. Typically, one or more SCs of the more than 250 categories are assigned to a given journal.

The scientific research landscape maps were constructed as follows. First, we harvested the publications indexed in the WoS database of the 17 research centers, including the WPI-iCeMS and the Wyss Institute, listed in Table 2.

[Table 2 here]

These organizations are regarded as being comparable to the research center to which one of the authors belongs. In the selection of these organization, the support of experts was sought. Articles, proceedings, and reviews from the year of their establishment up to 2014 were collected for each of these research centers. To focus on relevant SCs, a threshold ≥ 0.02 was set on the frequency of the SCs normalized by the total of the publications of each research center. This threshold represents the average of the third quartile of the normalized SCs of the research centers. Moreover, to get around the generality of the SC "Multidisciplinary Sciences," articles with this SC were allocated two to four relevant SCs from their list of cited references. Then, the Pajek software (De Nooy et al., 2011) was used to visualize the two-mode network that arises from the interconnections between the research centers and their relevant SCs. The network layout was rearranged with the Kamada-Kawai layout algorithm with circular starting positions. Finally, the nodes of the network were colored according to the classification of the field of science and technology proposed by the OECD (OECD, 2007). In this classification scheme, science and technology fields are classified into 42 specific categories. The mapping of the classification of the WoS' SCs into the OECD's specific categories was used in this paper.

4.1.2. Meso level of analysis: Science overlay maps

Science overlay maps describe the meso-level in the analysis of knowledge integration. Developed by Leydesdorff and Rafols (2009) and Rafols et al. (2010), this bibliometric technique locates the bodies of research of organizations within the global structure of science. This method relies on a basemap built by the cosine-normalization of the cross-citation relationships between journals in terms of their subject categories. These normalized cross-citation interactions are regarded as approximations of the cognitive distances between scientific disciplines. In this approach, visual representations of the diversity and coherence of bodies of knowledge are obtained by the superimposition of the basemap with a layer of nodes depicting the scientific disciplines of a given research center (i.e. diversity), as well as the interactions between these disciplines (i.e. coherence).

The research methods for the construction of the science overlay maps are based on Rafols (2014) and Rafols et al. (2012). Rafols and colleagues have made a toolkit for building science overlay mappings publicly available (http://www.leydesdorff.net/overlaytoolkit/). Following these procedures, the diversity and coherence of the bodies of research for the WPI-iCeMS and the Wyss Institute are visually and quantitatively captured. For the case of diversity, this approach results in the superimposition on the basemap of nodes with sizes that vary according to the frequency of the relevant scientific disciplines of a given research center. Similar to the previous section, the journal subject categories are used as proxies for the scientific disciplines. By assessing differences in the intensity, number, and distribution of these scientific disciplines, insights into the diversity of the institute's research bodies can be gained. To focus on relevant disciplines, normalized frequencies of SCs to the total of articles greater than or equal to 0.30% are used following the literature (Rafols, 2014; Rafols et al., 2012). In this study, the commonly used Integration Index (I), also referred to "Rao-Stirling diversity," is used as a measure of diversity (Rafols et al., 2010):

$$I = 1 - \sum_{i,j} p_i p_j d_{ij}$$
^[1]

where p_i and p_j refer to the relative share of references citing the subject categories (SC) i and j, respectively, and d_{ij} defines the degree of relatedness between the SC i and j as given by their cosine similarity measure. Here, higher I values reflect greater levels of diversity. It is well-known that the I index captures a broader picture of the diversity phenomenon than do other measures by simultaneously considering variety, balance, and disparity-related issues in their calculation (Rafols, 2014). Additionally, Shannon's entropy was used as an alternative measure of knowledge integration (Hinze and Grupp, 1992):

$$S = -\sum_{i} p_{i} \ln p_{i}$$
^[2]

in which, similar to Equation 1, pi refers to relative share of references citing a given SC.

For the case of coherence, the cross-citations (i.e. the citing-cited relationships between publications) based on their SCs are used. For this purpose, SCs are extracted from the source publications and their list of references. To do so, a thesaurus relating the list of journals indexed in the WoS database with their SCs was applied to the data. This procedure was conducted using VantagePoint software (Porter and Cunningham, 2004). As proposed by Rafols et al. (2012), the evaluation of coherence attempts to capture the level of interaction between the relevant scientific disciplines of a given research center. Quantitatively, coherence (C) is defined as follows (Rafols, 2014):

$$C = \sum_{i,j(i\neq j)} p_{ij} d_{ij}$$
^[3]

where p_{ij} defines the proportion of citations between the subject categories i and j, and d_{ij} defines the degree of relatedness between the SC i and j as given by their cosine similarity measure. Graphically, coherence can be assessed by comparing the cross-citations, as given by their SCs, *observed* for a particular research entity with those that should be *expected* based on the scientific interrelations of the global science map (Rafols, 2014; Rafols et al., 2012). Superimposing the basemap with those cross-citation relationships with observed-vs-expected ratios above a certain threshold (in our case 3.5) reveals the relevant interconnections between disciplines. To focus on relevant interrelations, cross-citations with weights higher than 0.15% were assessed. These thresholds were empirically determined to fit the data from both research centers.

4.1.3. Micro-level of analysis

The mapping approaches described so far have approached knowledge integration at a disciplinary level. However, interdisciplinary efforts can be visualized from deeper levels of analysis by using term maps and related mapping approaches.

4.1.3.1. Term maps and density maps

Term maps, also referred to as "co-words maps," have a long history in bibliometrics. The earliest efforts in this field date back as far as the 1980s in the work of Callon and colleagues (Callon et al., 1983). Term maps refer to the two-dimensional representations of the associations that arise from the co-occurrence of terms in scholarly articles. The more often these terms appear together in a document (i.e. co-appear), the stronger their degree of association. The stronger the degree of association between them, the closer they tend to appear on the term map. For us, term maps represent the cognitive networks underlying the scientific activities of research centers.

Term maps are constructed as follows. First, terms are extracted from the relevant documents of the WPIiCeMS and Wyss Institute. Although this study relied on data from the WoS database, we used the Scopus database for the harvesting of relevant terms. The Scopus database provides a wider range of indexed terms (e.g. MESH, EMTREE terms) than does the WoS database. An exhaustive parallel procedure was conducted to review each scholarly article manually in order to define additional relevant terms from their titles, abstract, introduction, and conclusions. This was followed by iterative cleaning and grouping procedures on the selected terms. Terms with frequencies greater or equal to three were assessed. To consider differences in the sizes of research groups, frequencies greater or equal to two were considered for those PIs with fewer than 10 publications in the time periods considered in this study. These thresholds were empirically determined to approximate the structures of these research centers.

After applying these thresholds, 1,498 and 947 terms were obtained for the WPI-iCeMS and the Wyss Institute, respectively. Three time periods were considered: up to 2010, 2011 to 2012, and 2013 to 2014. For each time period, matrices quantifying the co-occurrences of terms were built with VantagePoint software (Porter and Cunningham, 2004). Following the literature, a cosine-normalization was applied on the cooccurrence values of these matrices. To focus our attention in relevant interconnections, a threshold greater or equal to 0.18 was set on the cosine-normalized matrices. Cosine thresholds between 0.10 and 0.20 are common in the literature (Ávila-Robinson and Miyazaki, 2013). The visualization of these matrices was conducted using Pajek software. Two types of layouts are used for the visualization of these matrices: graphand distance-based maps. Although graph layouts tend to be more readable and aesthetically pleasing, the distances between nodes need not correspond to the strength of the relations between items; for this, distance layouts are used (Borgatti et al., 2013; Van Eck and Waltman, 2010). The Fruchterman-Reingold algorithm was used for the case of the graph layout, and the mapping approach embedded in the VOSviewer software was used for the distance layout approach. VOSviewer was also used to extract the clusters of highly interconnected terms from the term maps. For the Fruchterman-Reingold graph layout, the Kamada-Kawai layout was used as a seed layout to account for their high sensitivity to the starting position of nodes. For the graph- and distance-based layouts, we used a minimum cluster size of 15 and a cluster resolution of 2.0, which defines the level of detail of the clustering technique (Van Eck and Waltman, 2010). Given the lower number of publications for the Wyss Institute during the periods from 2009 to 2010 and from 2011 to 2012, minimum cluster sizes of 8 and 10 were used, respectively. This study used the density map visualization provided by VOSviewer. Through a red/green/blue color palette, the density map highlights important areas of the term map based on the number of neighboring items and their weights (Van Eck and Waltman, 2011).

4.1.3.2. Cluster maps

The mapping approaches described in Section 4.1.3.1 rely on matrices relating terms to terms. However, additional dimensions can be gained by converting the terms-to-terms matrices of Section 4.1.3.1 into matrices relating scholarly articles to scholarly articles. Following the cognitive emphasis of this study, two approaches were used in combination (Horlings and Gurney, 2013): paper co-word networks and bibliographic coupling networks. Paper co-word networks are derived from the matrices T_w that relate documents to their terms. Paper co-word networks are obtained by multiplying the matrix T_w with its transposed matrix T_w' . This gives paper-to-paper matrices relating scholarly articles with each other on the basis of the terms they share. Similarly, bibliographic coupling networks are estimated by multiplying the matrix T_b relating documents to their references with its transposed matrix T_b' . This gives paper-to-paper matrices relating scholarly articles based on the references they share. Similar to previous approaches, both paper co-word and bibliographic coupling networks were cosine normalized. Then, the

average of both matrices was calculated for each research center. Clusters were extracted from this hybrid matrix using VOSviewer software; 39 and 52 clusters were obtained for the Wyss Institute and WPI-iCeMS, respectively. In a subsequent step, the hybrid matrices of section 4.1.3.2 were combined into their clusters with the UCINET/NetDraw software leading to simplified networks relating clusters with clusters.

4.2. Bibliometric indicators

The mapping approaches of Section 4.1 were complemented with a series of bibliometric indicators. Following the literature, four main categories of bibliometric measures were used: knowledge integration-, cognitive-, collaboration-, and research impact-oriented bibliometric indicators. The specific indicators included in each of these categories are described below.

4.2.1. Knowledge integration

Two indicators were used to measure the degree of integration in the bodies of knowledge of research centers: the Rao-Stirling diversity index and Shannon's information entropy index. Both indexes are described in detail in Section 4.1.2.

4.2.2. Nature of scientific knowledge

Knowledge is characterized by different rubrics or natures. To determine the nature of the scientific knowledge generated by both research centers, three proxies are used:

- **Cognitive classification**: This indicator classifies articles according to the macro scientific disciplines they belong to using the classification scheme proposed by (OECD, 2007). In this classification scheme, science and technology fields are classified into 42 specific categories. The mapping of the classification of WoS' SCs into the OECD's specific categories was used in this paper.
- **Cognitive group**: The nature of scientific knowledge is also dependent on where the research efforts are occurring on the cognitive networks underpinning research centers. A proxy for this measure is given by the clusters allocated to the scholarly articles of the WPI-iCeMS and the Wyss Institute on the hybrid paper co-word/bibliographic coupling maps described in Section 4.1.3.2,.
- **Cognitive stage**: This measure describes the stage the research efforts embodied in scholarly articles have reached in the problem-solving sequences embedded in particular fields of research. "Problem sequences" are defined as the "recurrent patterns of problem search and solution" guiding research (Ávila-Robinson and Miyazaki, 2013; Metcalfe et al., 2005). To operationalize this measure, we defined the taxonomies of problem sequences involved in the main research fields of both research centers. The cognitive stage was simplified into three main stages: basic understanding, intermediary activities (e.g. synthesis of materials, development of component technologies), and downstream activities (e.g. application-oriented efforts regardless of their stage of development), as shown in the Supplemental Tables 1. Although the boundaries between these problem stages may be blurred, we believe that the "cognitive center of gravity" of articles tend to revolve around one of these stages. As these definitions are highly dependent on the field of study, an in-depth understanding of the different technologies is necessary for correctly tagging articles. For this, the technical literature and expert advice were consulted, as described in Section 4.3.

4.2.3. Collaboration

In this study, several measures were used to characterize the nature of the collaboration schemes of both research centers:

- Number of affiliated countries: This measure refers to the number of countries involved in a scholarly article. As such, it is used as a proxy for the degree of internationalization of a given article. Professorial appointments of faculty members in multiple countries were fractionalized for this measure.
- **Percentage of local co-authors**: This indicator refers to the percentage of coauthors affiliated with organizations geographically co-located with the research centers under study (i.e. the prefecture of Kyoto for the WPI-iCeMS and the state of Massachusetts for the Wyss Institute) regardless of the type of organization. In a sense, this measure defines the degree of locality of a scholarly article.

- Number of PIs: This indicator measures the number of PIs coauthoring a scholarly article. For the purposes of this measure, adjunct faculty and other faculty members under the PIs, such as assistant professors, associate professors, and lecturers are also included. The specifics of the calculation of this measure vary according to the organizational structure of each research center. For the Wyss Institute, for example, we included the additional organizational units of "Advanced Technology Team" and "Research Scientists & Engineers" as aggregate PIs. The "number of PIs" measure refers to the level of intracollaboration in a given scholarly article.
- **Types of co-authoring organizations**: This measure assesses the percentage of coauthors in a given article affiliated with firms and hospitals, respectively.

4.2.4. Research Impact

The assessment of the research impact of publications relies on their normalized citation impacts. For this measure, the raw citation counts of articles are divided by the appropriate ESI (Essential Science Indicators) baseline value provided by Thomson Reuters (as of September 2015). The ESI baseline values refer to the average performance measures of a group of articles within the same field, document type, and in a given year of publication (Thomson-Reuters, 2014). Self-citations are included.

4.2.5. Heatmaps of bibliometric indicators

Heatmaps were built to visualize the performance of research centers across the different bibliometric indicators mentioned above. The data were normalized through standardized z-scores by z = (value - mean of baseline data) / standard deviation of baseline data. By forcing each data sample to have mean = 0 and standard deviation = 1, it is possible to compare units of a different nature. To classify the datasets, a hierarchical clustering approach was conducted using SPSS software. This analysis relies on Ward's clustering method and squared Euclidean distances. The dendrograms obtained from this analysis were used to classify the dataset. To color the heatmaps, a color scale ranging from green (z-scores of -2 and below) to red (z-score of +2 and above) was used. For the visualization of the data into heatmaps, the Origin 2015 software was used.

4.3. Expert review

Qualitative review of the results of the bibliometric studies was conducted as follows. For the Wyss Institute a member of its management committee and a former postdoctoral student were selected as reviewers. In both cases, an hour-long semi-structured interview was conducted. The results of the interviews were complemented with publicly available sources of information, such as general articles about the Wyss Institute in journals and academic reports, press releases, and video media found online. For the WPI-iCeMS, the expert review consisted of presentations and discussions of the results to an audience of PIs and postdoctoral studies in two workshops. Additionally, progress reports, press releases, and additional internal documents were used to complement our results.

5. Results

Here we report the results on the research activities described in the conceptual framework shown in Fig. 1. This section presents the results of the bibliometric-based, network-oriented, and visualization-rich approaches used to explore the patterns of knowledge integration emerging from the practices and activities of interdisciplinary research centers.

5.1. Macro level: Positioning of research centers in the scientific research landscape

This research activity aims to locate research centers relative to each other based on their scientific makeup (i.e. the contents of their scientific knowledge bases). These relationships are visualized in the scientific research landscape maps, which refer to two-mode networks that relate the research centers listed in Table 2 (blue square-shaped nodes in Fig. 2) with their relevant scientific disciplines (circle-shaped nodes in Fig. 2).

[Figure 2 here]

As mentioned, the scientific disciplines of research centers are approximated by the journal subject categories allocated to the total of their scholarly articles. In Fig. 2, the scientific disciplines (circle-shaped nodes) are colored according to the OECD's general classification of macro scientific fields. In this figure, lines connect research centers to their relevant scientific disciplines, or scientific competencies. The thickness of these lines varies with the value of the normalized frequencies of the scientific disciplines of research centers. By dividing the scientific research landscape of Fig. 2 into general regions of science, we can observe two main poles— namely, the physical and life sciences, punctuated by patches of engineering and mathematical and computer sciences, to a lesser degree. The "positioning" of a research center within this map varies with the nature and intensity of its scientific competencies relative to those of other research centers. The more scientific competencies they share, the closer they appear on the map in Fig. 2.

The scientific research landscape map reveals a clear constellation of research centers. At one end, Fig. 2 shows a group of research centers with scientific competencies heavily influenced by life sciences domains, such as biochemistry and molecular biology, cell biology, biotechnology and applied microbiology, biophysics, biochemical research methods, and (partly) genetics and heredity. These research centers are the MIT's Whitehead Institute, Riken's CDB, Tata Institute of Fundamental Research's NCBS, University of Edinburgh's CRM, Max Planck's CBG, Princeton University's LSI, Tsinghua University's Center for Life Sciences, and MIT-Harvard University's Broad Institute. Besides their core disciplines, some of these research centers emphasize unique competencies: quantitative sciences by the LSI, biomedical domains by the Broad Institute, general biology domains at the NCBS, cell and tissue engineering at the CRM, and developmental biology by the CDB. At the other end, the scientific competencies of the Université de Versailles' ILV and the Lawrence Berkeley National Lab's Molecular Foundry appear to be significantly dominated by the physical sciences and partly by engineering. These research centers share interests among a set of core disciplines, such as physical chemistry, nanoscience and nanotechnology, multidisciplinary materials sciences, multidisciplinary chemistry, and condensed matter physics. Despite their similarities, the ILV focuses on basic fields of chemistry such as electrochemistry, crystallography, and inorganic and organic chemistry, while the Molecular Foundry is active in more applied disciplines such as nanotechnology, applied physics, materials science, and analytical chemistry.

A further examination of Fig. 2 reveals a set of organizations lying between both groups of research centers. The Scripps Research Institute's Skaggs Institute and to a lesser degree the Max Planck's IMP are characterized by scientific competencies cutting across the life and physical sciences. These research centers have similar scientific makeups that combine both the core life sciences domains mentioned above with physical sciences fields such as organic chemistry, medicinal chemistry, and multidisciplinary chemistry. Finally, another group of research centers appear to be building scientific competencies at the intersection of the life sciences, physical sciences, and engineering. These are Harvard University's Wyss Institute, MIT's Koch Institute, Arizona State University's Biodesign Institute, WPI-iCeMS, and to a lesser degree the UCLA and UC Santa Barbara's CNSI. The potential interdisciplinary nature of these research centers is reflected in their missions: bio-inspired engineering, integrative cancer research, nature-inspired research, integrated cellmaterial sciences, and nanosystems, respectively. Previous reports have highlighted the potential opportunities of research centers bridging multiple regions of science (MIT, 2016; NRC, 2014; Sharp and Langer, 2011). Given their scientific positioning, we expect potentially high interdisciplinary and converging natures for these research centers.

Thus, the positions occupied by research centers within the scientific research landscape provide initial insights, at the aggregate level of groups of research centers, into the patterns of knowledge integration efforts. This approach revealed the nature of the integrative scientific competencies of research centers. It was shown that the scientific positioning of research centers encompassed single to multiple macro-fields of research: physical, life, computational and mathematical, and engineering sciences. However, this approach overlooked the interconnections between the scientific disciplines of Fig. 2. These will be examined in the next section through the science overlay mapping approach. In the rest of this paper, the cases of the Wyss Institute and the WPI-iCeMS are emphasized.

5.2. Meso level: Positioning of knowledge bases within the whole of science and their characterization

This section uses the science overlay mapping approach, which locates the scientific competencies of research centers within the whole of science as a way to assess their diversity and coherence (Leydesdorff and Rafols, 2009; Rafols, 2014). Whereas diversity refers to the disparity, variety, and (im)balance of given bodies of knowledge, coherence describes the interconnections between them (Porter et al., 2007; Rafols, 2014). Fig. 3a shows the diversity of the research bodies at the WPI-iCeMS and Wyss Institute between 2007 and 2014 and between 2009 and 2014, respectively.

[Figure 3 here]

In Fig. 3, basemaps depicting the whole of science are superimposed with a set of nodes representing the relevant scientific disciplines of research centers as proxied by the journal subject categories of their scholarly articles. The sizes of these nodes vary according to the frequencies of the scientific disciplines normalized by the total of the scholarly articles of a given research center. Fig. 3 shows that both research centers display diverse and cognitively distant scientific disciplines. Interestingly, the scientific knowledge bases of both research centers are rather similar. These similarities can be further confirmed with the diversity-related measures the Rao-Stirling diversity and Shannon's entropy values, as shown in Table 3 (top).

[Table 3 here]

In line with the previous section, the scientific makeup of both research centers cuts across the life sciences, physical sciences, and engineering, including cell biology, biochemistry and molecular biology, biotechnology and applied microbiology, nanoscience and nanotechnology, multidisciplinary chemistry, physical chemistry, applied physics, and multidisciplinary materials science. Less intensely, both research centers explore the fields of physics, computer sciences, mathematical methods, and clinical medicine. Differences also appear, however. The Wyss Institute uniquely emphasizes engineering-oriented disciplines such as biomedical engineering, biomaterials, and robotics, while the WPI-iCeMS is characterized by its focus on inorganic chemistry, optics, medicinal chemistry, pharmacology and pharmacy, and, to a lesser extent, on oncology and developmental biology. For both research centers, the "Multidisciplinary Sciences" subject category is prominent, with shares of 19% and 7% for the Wyss Institute and WPI-iCeMS, respectively. As "Multidisciplinary Sciences" agglomerates multiple disciplines, it may lead to a loss of information. This is particularly important for leading-edge research centers as they tend to emphasize the publication of articles in high-impact journals, such as *Science, Nature, PNAS*, and *Scientific Reports*, which are usually classified as multidisciplinary by bibliographic databases.

Diversity does not assess the interactions between disciplines, however, which is a key feature of knowledge integration. This is done through the evaluation of coherence, for which we follow Rafols et al. (2012)'s approach. Basically, this method highlights higher-than-expected interactions between disciplines, which may be regarded as relevant and unconventional interconnections between them. To do so, the cross-citations between the source publications of a given research center and their cited references are defined in terms of their journal subject categories. These are referred to Rafols et al. (2012) as the "observed cross-citations". By contrast, "expected cross-citations" embody those cross-citations that would be expected to take place based on the interactions between disciplines drawn from the basemap. Interactions between disciplines above a certain ratio of observed vs. expected cross-citations are visualized in this figure. Fig. 3b shows these maps for both research centers. A more detailed display of the interconnections of Fig. 3b is shown in Fig. 4.

[Figure 4 here]

Although both research centers "overexpress" interactions bridging the life and physical sciences, the intensity of their knowledge integration efforts differs significantly. As shown in Fig. 4a, the Wyss Institute displays denser and more intense interconnections. What is more, the Wyss Institute's interactions involve more cognitively distant disciplines in the fields of clinical medicine (cardiac and cardiovascular systems, peripheral vascular diseases, and microbiology) and materials sciences (polymer science). In fact, the Wyss Institute displays 2.7 times more interconnections than does the WPI-iCeMS, as inferred from its higher

coherence values (see Table 3). Biomedical engineering and biomaterials appear to work as "connectors" between the life sciences and the physical sciences. Both disciplines account for almost half of all the relevant interactions in the science overlay map of Fig. 4a, signifying the pivotal intermediary role of engineering. As the lines of Fig. 4 are directed (i.e. they flow from the citing articles to their cited references), it is possible to evaluate disciplines according to their number of out-going or incoming lines. Whereas the former may be regarded, even if only approximately, as drivers of knowledge integration, the latter may be referred as the building blocks supporting knowledge integration. For the Wyss Institute, besides biomedical engineering and biomaterials, nanoscience and nanotechnology and chemistry (multidisciplinary) appear to be the driving disciplines behind knowledge integration (see Table 3, bottom). Based on the top-five scientific disciplines with the highest in-degree values (see Table 3, bottom), biology-oriented disciplines appear to be underlying the Wyss Institute's knowledge integration efforts.

By contrast, the WPI-iCeMS shows sparser and less intense knowledge-integrating relations (see Fig. 4b). In line with its mission, the WPI-iCeMS appears to be stressing interconnections between biological and materials science-oriented disciplines. The bulk of these interactions appears to be dominated by the discipline "chemistry, multidisciplinary," which tends to include journals approaching chemistry from an interdisciplinary perspective. In fact, half of the relevant interconnections interact with this discipline. Besides this, nanoscience and nanotechnology, materials science (multidisciplinary), and cell and tissue engineering are also significant drivers of knowledge integration at the WPI-iCeMS. Similar to the Wyss Institute, knowledge integration efforts at the WPI-iCeMS rely on biology-oriented disciplines such as biochemistry and molecular biology, cell biology, and biotechnology and applied microbiology (see Table 3, bottom). Compared to the Wyss Institute, the WPI-iCeMS displays stronger interconnections with physics-related disciplines such as Applied Physics and Physics, Atomic, Molecular and Chemical and with life sciences-related fields such as Developmental Biology and Pharmacology and Pharmacy.

Through the science overlay maps we can confirm that both research centers are actively breaking the boundaries between living and non-living systems (Ingber, 2011). However, the nature, intensity and drivers of their knowledge integration efforts varied considerably. Although this approach explores in greater detail the scientific makeup of research centers and their interconnections, it is still limited to the aggregate level of disciplines. There is thus a need to examine knowledge integration through the research projects and topics behind these scientific disciplines and their interconnections. The next section presents this approach with the use of term maps and other related methods.

5.3. Micro level: Exploration of the structure, dynamics, and contents of the cognitive maps

This section explores the patterns of knowledge integration of the Wyss Institute and the WPI-iCeMS at higher levels of granularity. To this end, cognitive maps are built. In doing so, this section clarifies the structure, dynamics, and contents of these cognitive maps, and reveals how these maps relate to the organizational forms of these interdisciplinary research centers.

5.3.1. Structure and dynamics of cognitive maps

Three types of visualization approaches are used to characterize the structure and dynamics of the cognitive maps of IDR centers (see Figs. 5a and 5b): graph layout-based term maps and their density visualizations (left and center, respectively), and the density visualization of the distance layout-based term map (right). As described, although graph layouts tend to be more readable and aesthetically pleasing, the distances between nodes need not correspond to the strength of the relations between items; for this, distance layouts are used (Borgatti et al., 2013; Van Eck and Waltman, 2010). Density visualizations are used to delineate the general structure of the cognitive maps, as well as to highlight their important regions of interaction (Van Eck and Waltman, 2011). As shown in Figs. 5a and 5b (center and right), the intensity of the interconnections within the cognitive structures is captured through a red/green/blue color scale: red denotes higher densities of interconnection between terms. For both research centers, three time periods are defined – up to 2010, 2011 to 2012, and 2013 to 2014 – to evaluate their dynamics of change over time.

[Figure 5 here]

The colors of the nodes of the term maps of Figs. 5a and 5b (left) correspond to those regions of high interaction between research terms, or clusters. These clusters are labeled according to the terms they contain. Contrasting the cognitive structures shown in Fig. 5a and 5b leads to some generalizations about the patterns of knowledge integration of both research centers. As can be observed in the visualizations of Figs. 5a and 5b. the cognitive structures of the WPI-iCeMS and the Wyss Institute vary considerably. Particularly, strong differences can be observed in the structures and distribution of their research contents across these maps. For the WPI-iCeMS, the density maps of Fig. 5a (center and right) denote a bipartite cognitive map. The cognitive contents of the WPI-iCeMS appear to be distributed as follows: a mostly physical sciences-oriented block on the left and a mostly life sciences-oriented block on the right. The former focuses on the synthesis of a diversity of materials (e.g. metal organic frameworks, organic compounds, perovskites, nanomaterials, and glycomaterials), while the latter emphasizes the understanding and manipulation approaches in different domains of cell biology (e.g. stem cells, neurobiology, germ cells, membrane biochemistry mechanisms). Additionally, the latter block embraces research efforts that appear to be integrating the physical sciences, life sciences, and engineering (e.g. cell imaging techniques, DNA nanotechnology, drug delivery approaches for chemo- and gene delivery). Interestingly, the results of Fig. 5a (center and right) reveal that both the life sciences- and the physical sciences-oriented blocks are getting closer over time. This may be attributable to the research efforts "bridging" the cognitive blocks.

By contrast, the cognitive structure of the Wyss Institute (see Fig. 5b, center and right) reveals a more fragmented or modular structure characterized by a wide range of topics across its cognitive map. The Wyss Institute's cognitive map is dominated by a highly connected region, or core, on tissue engineering-related topics (e.g., biomaterials and tissue scaffolds, therapies, and basic understanding) surrounded by a series of smaller yet intense regions on synthetic biology, antibiotic activity, cell engineering, and DNA nanostructures. The rest of the cognitive structure is characterized by several less-intense research domains not shown on the density maps, as they are overshadowed by other research streams. The general structure of the cognitive maps of the Wyss Institute can be defined as follows. The upper left region involves tissue engineering and the physical and life sciences in different degrees. The bottom left region of these maps consists mostly of life sciences-oriented domains, such as synthetic biology, systems biology and antibiotics, cell engineering and gene editing approaches. Finally, the right region of the map embraces physical sciences-oriented domains mostly related to the synthesis of materials, such as nanostructured surfaces, hierarchical structures, and adaptive materials.

5.3.2. Characterization of the contents of cognitive maps

Greater understanding of the particularities and specificities of the cognitive maps of Fig. 5 can be gained through their conversion into document-based networks (i.e. networks that relate "papers with papers" instead of "terms with terms"). The methods of constructing document-based networks are described in Section 4.1.3.2. For simplicity's sake, the nodes of these paper-to-paper networks are combined into their clusters leading to networks relating clusters with clusters (see Fig. 6). In these cluster networks, each node represents a group of highly interconnected scholarly articles on the basis of the terms and cited references they share. These clusters represent the "elemental" research domains along which a given research center channels its R&D efforts. In total, 39 and 52 research domains were obtained for the Wyss Institute and the WPI-iCeMS, respectively. Similarly, the colors of the nodes in Fig. 6 denote groups of related research domains. For visualization purposes, these are also encircled with the red dotted lines. In a sense, these "clusters of clusters" relate to the general research fronts of these research centers. Each of these research fronts is labeled according to the terms extracted from the publications they contain, as shown in the list of their representative keywords shown in Fig. 6 (right).

[Figure 6 here]

Building on the discussions of Section 5.3.1, we can relate the results of Fig. 6 to the R&D paths and organization of these research centers. The modular approach observed in the Wyss Institute results in three main poles: "tissue engineering and related fields", "synthetic biology and gene editing approaches", and "robot technologies, soft devices and non-linear dynamics/biological models". These are punctuated by the

intermediary research fronts "adaptive materials" and "DNA technologies". By contrast, the bipartite approach of the WPI-iCeMS is characterized as follows. There is a large group of research domains dealing with the "materials synthesis" (e.g. coordination, organic, inorganic, glycol-materials) on the right of Fig. 6 (bottom). At the other end, we observe a group of research domains on "stem cells" surrounded at a closer range by a series of cell-oriented research domains, such as "genetic switches", "drug delivery approaches", and "nanobio- and biophysical studies". Further away, "DNA nanotechnologies", "plasma membrane-related studies", and "cell imaging technologies" are located. Finally, "terahertz technologies" resides away from the rest of these research domains. Fig. 6 also reveals that despite the fragmented nature of the cognitive maps of the Wyss Institute, its research domains display greater levels of cognitive interaction than do those of the WPI-iCeMS, in line with the results of Section 5.2.

The differences in the structure and contents of the networks of Fig. 6 are strongly related to the forms of organization established by these IDR centers to carry out their R&D missions. For the Wyss Institute, Fig. 6 (top) closely resembles the "enabling technology platforms" underpinning its research organization. As described by Ingber (2011), technology platforms represent teams working on bio-inspired technologies focusing on certain application areas of interest. Six platforms have been defined: adaptive material technologies, living cellular devices, bio-inspired robotics, biomimetic microsystems, programmable nanomaterials, and synthetic biology. Faculty is allocated to one or more of these research platforms. By contrast, the WPI-iCeMS follows a more PI (principal investigator)-centered approach based on the establishment of independent research laboratories each dealing with the particular research interests of PIs (see Fig. 6, bottom). The fields to which PIs belong include nanobiotechnology, microfluidics, biophysics, stem cell biology, membrane biology, neurosciences, chemical biology, cellular biochemistry, terahertz optical science, germ cell biology, materials science, nanomaterial, and theoretical chemistry, among others. The differences between these models of research organization—by topic or discipline—though apparently subtle, are believed to significantly impact the way research centers extract value from knowledge integration (Huutoniemi et al., 2010; Siedlok and Hibbert, 2014; Stehr and Weingart, 2000), as the next section will show.

By characterizing the contents of the cognitive maps of Fig. 6, it is possible to gain deeper insights into the patterns of knowledge integration in the practices of IDR centers. We first examine this in Fig. 7 by mapping the levels of interdisciplinarity and the cognitive stage of the research domains of Fig. 6 for both research centers. Whereas interdisciplinarity is measured through the Rao-Stirling index of the research domains (see Section 4.1.2), the assessment of the cognitive stage is based on the stage of problem-solving embodied in their scholarly articles, as described in Section 4.2.2. The maps of Fig. 7 show statistically significant relationships between both measures, as inferred from the correlation matrices of the Supplemental Table 2. This is line with the differences of interdisciplinarity observed across different research contexts (Frodeman, 2011; Sanz Menéndez et al., 2001; Van Rijnsoever and Hessels, 2011). However, the patterns of distribution of research domains differ widely in these maps. The Wyss Institute (see Fig. 7, left) shows higher levels of interdisciplinarity and a greater tendency to engage in "downstream" (application-oriented) R&D efforts than the WPI-iCeMS (see Fig. 7, right). This is to be expected given the engineering- and translation-oriented nature of the Wyss Institute; yet, Fig. 7 provides the full portfolio of research domains. There are some exceptions, such as the synthesis of inorganic materials and the development of terahertz technologies in the WPI-iCeMS. Despite their "basic research" connotations, these fields of research show high levels of interdisciplinarity through the close integration of chemistry and physics.

[Figure 7 here]

Continuing with the characterization of the contents of the cognitive maps in Fig. 6, we mapped the 39 and 52 research domains obtained for the Wyss Institute and the WPI-iCeMS, respectively, across the bibliometric indicators of Section 4.2. These include cognitive-, collaboration-, research impact-, and diversity-related measures. To visualize these data, heatmaps were built for both research centers (see Fig. 8), as described in Section 4.2.5. The rows of these heatmaps are arranged on the basis of hierarchical clustering approaches, as shown in the dendrograms placed at the left of both heatmaps of Fig. 8. On the right of these heatmaps, we find the list of research domains, the nodes of Fig. 6, and the research fronts, the group of nodes encircled with red dotted lines in Fig. 6. The colors on the list of research domains refer to the research fronts of Fig. 6.

[Figure 8 here]

Fig. 8 reveals distinctive patterns in the distribution of the research domains of Fig. 6 on the basis of the intensities of their bibliometric indicators across the heatmaps. Five and nine macro-groups sharing particular combinations of bibliometric measures were obtained for the Wyss Institute and the WPI-iCeMS, respectively. Fig. 8 shows that research domains from similar research fronts tend to group together in similar macrogroups. This suggests that research domains are not only cognitively intertwined as inferred from the networks of Fig. 6, but also share similar properties as inferred from the heatmaps of Fig. 8. These groups of research domains are characterized by specific patterns of common properties, (i.e. research trajectories, across cognitive, collaborative, impact-related, and integrative measures). For both research centers, the macrogroups of Fig. 8 show strong dependences on specific fields of science and technology: life sciences, physical sciences, engineering, mathematical sciences, and computer sciences. For the WPI-iCeMS, Fig. 8 shows the high degrees of internationalization of the research domains "nanobiotechnology" and "stem cells". On the contrary, "genetic switches," "organic materials," and "terahertz technologies" rely heavily on researchers colocated in the Kyoto prefecture. Others such as "imaging technologies," "drug delivery systems," and "plasma membrane studies" tend to stress intra-collaboration schemes among WPI-iCeMS' PIs. Moreover, whereas "coordination materials (MOF/PCP)" and "terahertz technologies" tend to collaborate with firms, "stem cells" and "drug delivery systems" do so with hospitals. For the case of the Wyss Institute, "microfluidic devices," "tissue engineering, biomaterials," and "tissue engineering, mechanotransduction" show the greatest levels of internationalization. In contrast, "adaptive materials," "gene editing," "soft devices," and "tissue engineering, cardiovascular" tend to rely on collaborations with researchers co-located in the Massachusetts area. Besides "soft devices" and "tissue engineering, mechanotransduction", the research domain "microfluidic devices" shows the greatest levels of intra-collaboration among the Wyss Institute's faculty. Whereas "tissue engineering, drug delivery" is characterized by high interactions with firms, "microfluidic devices," "tissue engineering, biomaterial," and "tissue engineering, mechanotransduction" denote stronger clinical orientations through their close interactions with hospitals. These relationships can be corroborated with the correlations in Supplemental Table 2. As inferred from these results, the practices of IDR centers reveal heterogeneous patchworks of research domains characterized by multiple research trajectories. Regarding their propensity for knowledge integration, two general patterns can be drawn from Fig. 8: interdisciplinarity-enabling and interdisciplinarity-generating research domains. The former tends to focus on the creation of mostly monodisciplinary, basic understanding and intermediary knowledge, such as the synthesis of materials and the development of basic technologies, which, through subsequent recombination efforts may lead to interdisciplinarity-oriented knowledge. The latter tends to target more downstream areas of problem solving, mostly devices or solutions oriented to applications, with high levels of interdisciplinary knowledge.

In summary, this section analyzed the patterns of knowledge integration at greater levels of granularity. By studying the structure, contents and dynamics of the cognitive maps of research centers, we could reveal differences between and, more importantly, within these organizations. The realities of the practices of interdisciplinary research centers display heterogeneous patchworks of research domains driven by multiple research trajectories—some enabling, and others generating interdisciplinary knowledge. As the next section explains, an understanding of these differences has implications for the management and organization of knowledge integration.

6. Discussions and Implications to policy, practice and theory

6.1. Key findings of this research

The complexity of the problems and challenges faced by researchers and scientists is calling for solutions that cut across multiple and cognitively diverse disciplinary domains. We succeeded in demonstrating, at different levels, perspectives, and granularities, the patterns of knowledge integration emerging from the practices and activities of IDR centers. At the macro level, our approach revealed the nature of the integrative scientific competencies of research centers. We could see how the scientific positioning of research centers encompassed single to multiple macro-fields of research, from the physical, life, computational and mathematical, and engineering sciences. From the meso-level perspective, we demonstrated that the Wyss

Institute and the WPI-iCeMS were actively breaking the boundaries between living and non-living systems. Yet, the makeup of knowledge interconnections of both research centers differed significantly on the basis of their natures and intensities. The Wyss Institute appears to be mostly driven by application-oriented fields such as biomedical engineering, biomaterials, and nanotechnology, while the WPI-iCeMS tends to rely on the more basic-oriented fields of chemistry, materials sciences, and biology. The greatest differences were captured through the micro level. Different topologies were observed for both research centers: fragmented or modular for the Wyss Institute, bipartite for the WPI-iCeMS. The practices of both IDR centers were denoted by heterogeneous patchworks of research domains driven by multiple research trajectories. From these findings, implications to the policy, practice and theory of IDR centers are presented below.

6.2. Implications to theory

This study contributes to the literature on interdisciplinarity in three ways. First, we propose to study knowledge integration in the practices and activities of IDR centers using a multilevel, integrated approach. Indeed, this approach has been suggested previously for the science of team science (Börner et al., 2010), but it has neither been advanced nor empirically developed in the context of IDR centers. Our findings indicate that such approaches are appropriate for addressing the multi-dimensionalities, complexities, multiple levels of aggregation and granularity, and different perspectives inherent in interdisciplinary research (Cambrosio et al., 2006; Klein, 2008; Rafols et al., 2012; Rafols and Meyer, 2010; Sanz Menéndez et al., 2001). Our study also provides a more realistic conceptualization of the practices of IDR centers. Beyond the idealizations of full convergence common in the literature, we visualize IDR centers as patchworks of research domains driven by diversified research trajectories—some indirectly enabling, others directly generating interdisciplinary knowledge to different degrees. These results reveal the complementary roles of disciplinary and interdisciplinary knowledge, as inferred by others (Jacobs, 2013; Repko, 2008; Siedlok and Hibbert, 2014; Stehr and Weingart, 2000). We would expect disciplinary research efforts to catalyze into interdisciplinary research through their recombination with additional sources of knowledge, for example, as seen in the multi-directional chains of understanding (i.e., basic or discovery-oriented) and manipulation (i.e., problem- or application-oriented) in the case of science research. Studies have highlighted that interdisciplinarity is not an end in itself but a means to an end-namely, the advancement of knowledge through solutions to complex problems (Frodeman, 2011; Jacobs, 2013). The need to not overlook the whys for the hows of interdisciplinarity has also been highlighted, emphasizing the "... underlying impulses behind the push for interdisciplinarity approaches to knowledge production" (Frodeman, 2011). Our results have shown that the "impulses" of interdisciplinary research in science are strongly driven by the types of research problems facing IDR centers (NRC, 2014), which in turn should be intimately related to their respective missions. Consequently, the level of interdisciplinarity in a research center assumes a secondary role; instead, stakeholders associated with the research should question the extent to which their efforts fulfil the highly interdisciplinary-oriented missions of their IDR centers, the main impulse behind knowledge integration.

Second, this study provides empirical evidence on the role of the heterogeneities of knowledge integration in the research management of IDR centers. Many authors have highlighted the social, cognitive and physical boundaries and contexts delimiting different fields of research (Battard, 2012; Heimeriks, 2013; Sanz Menéndez et al., 2001; Van Rijnsoever and Hessels, 2011). Differences in knowledge integration certainly occur, not only in between but also (and more importantly) within IDR centers. Our results highlight the need for understanding the cognitive makeup of IDR centers for the effective fostering of interdisciplinarity. We show that the heatmaps in Fig. 8 are practical tools for understanding at a glance the particularities and specificities of IDR centers on the basis of their disciplines, cognitive nature, collaboration schemes, impact, and levels of knowledge diversity. Certainly, these studies should be expanded to include the greater contexts within which IDR centers function. Given these differences, we would expect that numerous ways or modalities of bringing about integrated knowledge exist (Battard, 2012; Huutoniemi et al., 2010; Klein, 2008). As pointed out by NRC (2014), the larger differences in size, missions, and available budgets preclude the definitions of single "recipes" for effectively facilitating interdisciplinary research. Thus, in regard to interdisciplinarity, "one size does not fit all." Our findings show that research stakeholders should deploy tailored and targeted strategies, instead of "all encompassing" ones, tuned to the specific characteristics of the particularities and specificities of IDR centers. In addition, our results expand the research management of IDR centers by redirecting their unit of analysis from disciplines to clusters, or research domains, which make up their cognitive structures. The results of this paper also demonstrate that observing the properties of these research domains and their interconnections can improve the understanding of research stakeholders, and thus, provide them better opportunities to channel their research efforts along their respective interdisciplinary missions.

Third, our study empirically demonstrates the impact of organizational structures on the effectiveness of IDR centers toward fulfilling the interdisciplinary missions for which they have been established. This is reflected in the different bibliometric mapping approaches employed in this paper. Our findings demonstrate that the "enabling technological platform-based" approach followed by the Wyss Institute appears to foster interdisciplinary research more effectively than the conventional principal investigator-centered approach of the WPI-iCeMS. We regard such modular approaches as more suitable for coping with the complexities of knowledge integration as they provide IDR centers with a sense of direction (even if at higher levels) of the pathways along which to channel their integrative efforts. This point has also featured in the NRC (2014)'s report, which notes the need for IDR centers to organize their missions around common themes, problems, or scientific challenges so as to foster knowledge integration. The differences between these research centers are widened by the organizational structure of the Wyss Institute, which is based on "colaboratories," wherein groups of people from different faculties work together within the context of a project or a specific application (Ingber, 2011, 2013). This contrasts with the organizational scheme of the WPI-iCeMS, wherein faculties have independent laboratories. We infer that the differences between the organizational structures of both IDR centers may be due to cultural differences in their ways of approaching integrated research management (Shibayama et al., 2015).

6.3. Implications to policy and practice

The results of this study provide research stakeholders with a series of practical recommendations for planning and assessing knowledge integration in IDR centers. First, the visualization approaches of this paper are not regarded as end goals in themselves but rather as points of departure from which to enrich discussions among scientists, analysts, policy makers, and reviewers about interdisciplinary research (Milojević et al., 2012). In particular, the visibility provided by the bibliometric mapping approaches used in this paper offers scientists and researchers greater opportunities for accessing, discussing, valuing, and managing the knowledge produced by research centers (Eppler and Burkhard, 2007; Sparrow, 1998). This is of great importance, as scientists tend to become so focused on their own research that they usually fail to grasp the "bigger picture" within which their research is embedded.

Second, as research becomes more complex, we foresee the continued use by research stakeholders of empirically grounded tools for R&D management, such as those presented in this paper. Of interest is their use as planning and assessment tools for practically and systematically understanding the effects of managerial decisions on knowledge integration efforts (Anzai et al., 2012). By considering these needs for the assessment and evaluation of interdisciplinary research, our study reveals cues for effective research management at multiple levels of the analysis, as demonstrated in the synthetic model presented in Fig. 9.

[Figure 9 here]

The macro-level visualization approach embodied in the academic research landscapes of Section 5.1 provides an overall perspective of the portfolio of R&D projects (or institutions) within a policy program. This level of analysis evaluates projects against other programs or projects on the basis of their scientific positioning and the quantity/quality of scientific outcomes according to the research program's goals. The meso-level visualization approach, as depicted by science overlay maps, can be used for the selection, development and evaluation of research centers on the basis of the project's overall mission and value proposition (see Section 5.2). Finally, the micro-level visualization approach using term maps and related methods (see Section 5.3) provides a prospective view of the networking possible among various research topics and potential collaborations. This level gives the heads of research labs useful insights into exploring, planning, and calibrating their research directions in accordance with the strategic goals of their respective research centers. Additionally, these three visualization approaches can be used for any level of research management. For instance, the macro or meso-level visualizations may help PIs understand the overall trends of their research programs or centers in a top-down manner. Micro-level visualizations may assist the program director or officers at the policy-making level to pursue emerging research topics and calibrate or renew the program design in a bottom-up manner. Notably, it becomes possible to not only acquire periodic data from affiliated researchers, but also to understand the current situation and discuss improvement plans during institute management decision-making on these indicators. For example, initiating a PDCA (plan-do-check-act) cycle of R&D activity could contribute toward systematic and continuous improvement of processes and activities, especially in applied research and/or interdisciplinary research, which involves the participation of numerous researchers from different institutions or academic fields. Certainly, these discussions do not overlook the fact that interdisciplinarity may often arise from unexpected, spontaneous interactions between researchers and scientists, instead of fixed R&D plans.

Third, the approaches in this paper can also be helpful in review processes. It is well known that reviewers often lack the necessary competencies to properly assess research centers dedicated to interdisciplinarity (Anzai et al., 2012). Moreover, the research centers under review may encounter difficulties in effectively conveying their performance and functionality to a reviewing committee. Review processes should be regarded as information-asymmetric situations in which research centers are certainly more capable of effectively assessing their own performance, including interdisciplinarity and knowledge integration, than a team of reviewers. In this regard the provision of empirically based analytical tools to reviewers can diminish the information asymmetries inherent in review processes.

6.4. Limitations of this study

This study has three main limitations. First, as with any research technique, bibliometric-based approaches have inherent limitations including (a) their inability to take into account R&D efforts that do not lead to publications; (b) their tendency to be highly sensitive to the inherent differences and specificities among research fields; (c) their limitation to publications indexed in the WoS database; (d) the well-known differences in referencing behaviors across research fields, such as the intensive use of conference proceedings by computer science or robotics; and (e) the difficulty of discerning the real relevance of a given scholarly article for a research center. Despite their imperfect nature, however, these approaches embody reproducible, informed and evidence-based approximations of reality complementing, not supplementing, R&D decision processes (Anzai et al., 2012). Second, given the nature of our approach, this paper is limited to the study of interdisciplinarity from a cognitive perspective, (i.e. the diversity of the knowledge being integrated by research centers). Although some collaboration-related measures were considered, we largely overlooked the social dimension of interdisciplinarity, (i.e. the diversity of the team of co-investigators). Social-oriented interdisciplinarity demands an estimation of the scientific and technological competencies of the set of co-authors of scholarly articles- methodologically, a daunting challenge. Social aspects appear to play an important role in the perceptions of interdisciplinarity by researchers—in the case of the research center of one of the authors, a qualitative self-assessment by the PIs on the level of interdisciplinarity of their scholarly articles against the bibliometric, (i.e. quantitative,) indicators used in this paper. It was found that scientists tended to overstress, by up to three times, social diversity (diversity of the team of co-investigators) relative to cognitive diversity (the diversity of the knowledge being integrated) in their perceptions of interdisciplinarity. Third, we have considered only the cases of two research centers in this study. However, this selection relied on archetypal research centers established with explicitly interdisciplinary aims, both of fairly similar sizes and working in similar fields of research. Given the generality of our approach, we believe that it can be transferred to other research centers active in different fields of science and technology.

7. Conclusions

As research becomes increasingly complex, the need to understand research centers, particularly those created with an interdisciplinarity spirit in mind, becomes more urgent. This study involved the use of multiple visualization and quantitative approaches to pragmatically examine the patterns of knowledge integration emerging and the forms of research organization from the practices and activities of interdisciplinary research centers. A multilevel approach including three approaches was used: the scientific positioning and makeup of research centers (macro level), the location of their scientific competencies within the whole of science (meso-level), and the characterization of the structure, dynamics, and contents of their cognitive maps (micro-level).

The cases of two interdisciplinary-oriented research centers were empirically evaluated: the Wyss Institute at Harvard University and the WPI-iCeMS at Kyoto University. The similarities in scientific positioning of both IDR centers at the macro-level translated into differences in the natures, intensities, and drivers of their knowledge interconnections at the meso-level. Beyond idealized conceptualizations of full convergence, the realities of IDR centers were characterized by heterogeneous patchworks of multi-trajectory research domains at micro levels—some of these indirectly enabling, others directly generating interdisciplinary knowledge, to different degrees. We observed that approaches to knowledge integration vary between but also, and more importantly, within IDR centers. The exploration and understanding of these inter- and intra-organizational differences proves crucial for effectively fostering knowledge integration. Several implications expected to contribute to the multilevel, pragmatic, and systematic assessment of research management, organization, and assessment of IDR centers were drawn from this study. Future efforts should be aimed at enhancing the approaches presented in this paper on two dimensions: (i) the use of additional sources of information, such as patent applications, internal project data, or grant applications, and (ii) the inclusion of additional case studies. This will widen the dimensions and perspectives of this paper.

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	Institute for Integrated Cell-Material Sciences (WPI-iCeMS)	Wyss Institute for Biologically-inspired Engineering (Wyss Institute)
Foundation year	2007	2009
Funding organization	Ministry of Education, Culture, Sports, Science, and Technology (MEXT) World Premiere International Research Center Initiative (WPI)	Private donation (Hansjörg Wyss)
Host institution	Kyoto University, Japan	Harvard University, United States
Core / adjunct faculty	26 / 17	19 / 12
Total research staff	246 (as of 2015)	~350 (as of 2014)
Approx. room space	11,000 m ²	9,290 m ²
Mission	To manipulate cell fate and functions with synthetic molecules: (1) nucleus information, (2) membrane compartments, and (3) cell communication	To discover the engineering principles that nature uses to build living things, and harness these insights to create biologically inspired materials and devices that will revolutionize healthcare and create a more sustainable world
General fields of research	Cell biology, chemistry, and physics	Engineering, medicine, biology, and physical sciences

 Table 1
 Comparison between WPI-iCeMS and Wyss Institute as of 2014 (based on publicly available information)

Institute	Host institution	Country	Earliest year	Total pubs
Biodesign Institute	Arizona State University	USA	2003	1,584
Broad Institute	MIT/Harvard University	USA	2004	4,417
California Nanosystems Institute (CNSI)	University of California Los Angeles (UCLA) and Santa Barbara	USA	2001	1,549
Center for Developmental Biology (CDB)	Riken Institute	Japan	2000	1,683
Center for Life Sciences (CLS)	Tsinghua/Peking Universities	China	2011	548
Centre for Regenerative Medicine (CRM)	University of Edinburgh	UK	2006	354
Institute for Molecular Cell Biology & Genetics	Max Planck Institute	Germany	1998	1,548
Institute for Molecular Physiology	Max Planck Institute	Germany	1993	1,842
Institute Lavoisier	Université de Versailles	France	1993	1,211
Koch Institute for Integrated Cancer Research	MIT	USA	2008	1,129
Lewis Stigler Institute for Integrated Genomics (LSI)	Princeton University	USA	2002	690
Molecular Foundry	Lawrence Berkeley Natl Lab	USA	2004	697
National Centre for Biological Sciences (NCBS)	Tata Institute of Fundamental Research	India	1992	1,039
Skaggs Institute for Chemical Biology	Scripps Research Institute	USA	1996	3,978
Whitehead Institute	MIT	USA	1982	4,068
WPI-iCeMS	Kyoto University	Japan	2007	1,189
Wyss Institute	Harvard University	USA	2009	887

 Table 2
 List of comparable research centers

	Measures	Wyss Institute	WPI-iCeMS
Diversity and coherence measures	Diversity (Rao- Stirling)	0.61	0.59
	Shannon's Entropy Coherence	3.14 0.48	3.26 0.36
In-degree/Out- degree disciplines	Top-five out-degree scientific disciplines [drivers] Top-five in-degree scientific disciplines [building blocks]	 Engineering, Biomedical Materials Science, Biomaterials Multidisciplinary Sciences Nanoscience & Nanotechnology Chemistry, Multidisciplinary Cell Biology Biochem & Molecular Biology Biotech & Applied Microbiology Multidisciplinary Sciences Chemistry, Multidisciplinary 	 Chemistry, Multidisciplinary Multidisciplinary Sciences Nanoscience & Nanotechnology Materials Science, Multidisciplinary Cell & Tissue Engineering Biochem & Molecular Biology Biotech & Applied Microbiology Cell Biology Cell Biology Physics, Condensed Matter Energy & Fuels

 Table 3
 Comparative table of indicators extracted from science overlay maps



Fig. 1 Analytical framework for the understanding of knowledge integration







Fig. 3 Knowledge diversity and coherence for the WPI-iCeMS and the Wyss Institute



Fig. 4 Relevant scientific interconnects for a) the Wyss Institute and b) the WPI-iCeMS



Fig. 5 Cognitive maps over the years for a) the WPI-iCeMS and b) the Wyss Institute



Fig. 5 Cognitive maps over the years for a) the WPI-iCeMS and b) the Wyss Institute (cont)



Fig. 6 Cluster networks for the total of publications, Wyss Institute (top) and WPI-iCeMS (bottom)



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- **: correlation statistically significant at the 0.01 level (2-tailed)
- Fig. 7 Relationships between the level of interdisciplinarity and the cognitive stage for the Wyss Institute (left) and the WPI-iCeMS (right)



WPI-iCeMS, 2007-2014

PHOTOVOLTAIC

CI 1145

authors from hospitals; NORM_CITATION: normalized citation

Fig. 8 Heatmaps of cognitive domains vs. bibliometric indicators for the Wyss Institute (left) and the WPIiCeMS (right)

Wyss Institute, 2009-2014



NOTES: The columns correspond to the three levels of visualization (micro, meso and macro). The rows correspond to the levels of research management that consist of the research programs governing multiple research centers, research centers alone, or multiple research labs or groups. The colored cells in the 3x3 matrix signify main areas of implementation of visualization approaches to management. The dotted arrows indicate potential influence of each visualization approach to other levels of management.

Fig. 9 Strategic matrix for the assessment of knowledge integration in IDR centers

Supplementary Tables 1

a) Wyss Institute

	STAGE 1	STAGE 2	STAGE 3
Field	Basic understanding	Preparative activities	Scientific/Clinical Applications (principles, proof-of- concepts, etc.) Includes also instrumentation/imaging techs, software
Angiogenesis	 Understanding/insights into natural angiogenesis Understanding the role of growth factors Understanding of the role of chemotactic gradients, cell adhesion and cell recruitment in angiogenesis 		 Therapeutic interventions for the treatment of ischemia/ischemic disease Building of vascular networks in animal models
DNA	Basic understanding	 Design, construction and assembly of 2D/3D DNA/RNA origami structures and their modification/functionalization (chemical, enzymatic and biophysical phenomena) 	 Single molecule visualization/imaging and biophysical analysis of biomolecules in DNA nanostructures Molecular machines/robotics Living cell analysis Therapeutic applications/drug delivery approaches based on DNA nanostructures DNA storage approaches Others uses of DNA/RNA nanostructures, e.g. NMR alignment, etc.
Synthetic biology	Basic understanding	 Demonstration of synthetic biological design approaches, e.g. switches, oscillators, Metabolic pathway 	 Devices and systems addressing specific application domains (biology, energy, pharmaceuticals, etc.)Synthetic circuits Signal transduction, protein-protein networks, metabolic networks
Non-linear	 Fundamental mechanisms of biologic control influencing the multiscale properties of complex systems 	 Methods to quantify multiscale properties of complex signals Novel indexes for risk stratification and monitoring of pharmacologic and non- pharmacologic interventions 	 Characterization of the complex behavior of physiological systems (diseases, etc.) Models of physiologic control Detection of diseases (sleep apnea,
Biomaterials		 Synthesis and characterization of biomaterials Photocrosslinkable biomaterials for surface patterning Development and characterization of nanofibers, nanotextiles, etc. 	 Generation of chemical gradients to study biomaterial-cell interaction Microwells for ECM-cell interaction
Microfluidics	Basic understanding (curling of wet paper)		 Organs on a chip: cardiac valve on a chip, muscle on a chip, HTS muscle on a chip HTS platforms Platforms for gradient microfluidics Controlled environments for stem cells
Drug delivery	 Quantitative understanding of spatiotemporal relationship between the drug and biological response (in-vitro) Mathematical modeling/simulation to predict drug delivery to target tissue 		 Drug delivery for therapeutic angiogenesis, bone regeneration, skeletal muscle regeneration, etc. (in-vivo, purposeful application [disease-oriented], etc.)
Robotics	 Experimental bio-mechanics Study of biological systems 	 Characterization of components, control techniques, etc. Development, characterization and modeling of soft fluidic actuators and their components (power, control, etc.) 	 Soft wearable robots Robotic prosthetics Exo-suits Flapping wing microrobots Microrobots (insect-inspired, myriapods, etc.): prototypes and dynamic models Printable/paper robots (origami-robots)
Immunotherapy	Understanding of the immune system		 Development of immunotherapies/ immunomodulatory therapies
Tissue engineering	 Mechanotransduction studies (impact of mechanical stress/strain, cell shape, cell architecture, etc. on cells) Molecular components or signaling pathways in mechanotransduction Studies on the relationships between electropropagation and cell architecture Studies on the mechanical coupling between cells Studies on the structure-function relationships in VSM pathphysiology 	 Development and synthesis of biomaterials Characterization of biomaterials (cell penetration, cell penetration, etc.) Development of muscular thin-films Approaches for the creation of micro-constructs to control cell organization, morphogenesis and formation Development and characterization of scaffold materials Demonstration of tissue constructs 	 How to use the effects of mechanics on cells in tissue engineering Approaches for the regeneration of musculoskeletal and dental tissues Cell transplantation approaches Tissue development Systems for growth factor delivery
Adaptive materials	 Understanding of Nature's concepts and the basic principles of biological architectures 	 Synthesis and nanofabrication strategies of materials 	 Devices and applications (architecture, energy efficiency, biomedical fluid handling, antifouling, etc.)

b) WPI-iCeMS

	STAGE 1	STAGE 3	
Field	Basic understanding	Preparative activities	Scientific/Clinical Applications (principles, proof-of- concepts, etc.) Includes also instrumentation/imaging techs, software
Pluripotent stem cells (ES, iPS, etc.) / Germ cells	 Definition of early lineage specification Basic biology of stem cells Epigenetic regulation of gene expression Regulation of gene expression and gene networks Regulation of the cell cycle Chromatin dynamics Spermatogenesis, germ cells RNA biogenesis of germ cells Mesenchymal cells Pluripotency-related studies Germ cell fate 	 Methodologies for the generation, expansion, and differentiation, etc. It also includes the understanding on these methodologies, e.g.: molecular determinants and mechanisms of differentiation and reprogramming, regulation of cell proliferation, signaling pathways for cell growth and differentiation, etc.) 	 Gene editing/targeting approaches Disease models Disease-specific stem cells Cell therapy approaches Regenerative medicine-related approaches (scaffolds, etc.) Research approaches Large-scale culturing methods Development of off-spring
Other cells	 Studies on morphogenesis, cytogenesis, etc. Meiosis Molecular mechanisms of cells Neurogenesis 	Characterization of cells (responses, stimuli, etc.)	
Developmental neurobiology	 Dynamics of neuronal migration Principles of dendrite branching Neurogenesis 		 Imaging techniques for the molecular analysis of neuronal motility
Biological physics	 Physics of cells and tissues Physics of biological, soft interfaces	 Composite materials (biomembranes and semiconductor devices) 	
	 Molecular mechanisms of epigenetics Study of the working mechanisms of biolmolecules (DNA, proteins, etc.) 		
Membrane	 Physiological roles of ABC transporters in cells Functional architectures of ABC transporters Mechanism of HDL formation Membrane mechanisms Molecular basis of membrane and membrane-protein dynamics 		
DNA	G-quadruplex properties	 Design, construction and assembly of 2D/3D DNA origami structures and their modification/functionalization (chemical, enzymatic and biophysical phenomena) Characterization of DNA (charge transfer, catalysis, damage, 	 Single molecule visualization and biophysical analysis of biomolecules in DNA nanostructures Molecular machines/robotics Living cell analysis Drug delivery approaches based on DNA nanostructures
Glycotechnology	 Elucidation of he molecular basis underlying the functions of carbohydrates 	 Synthesis of glycans (gangliosides, glycolipids, etc.) 	 Drug/gene delivery approaches Glycodirector systems Carbohydrate microarrays (glycomics) Diagnostic tools and disease biomarkers Labeling approaches (probes) Cancer migration, immune system, virus entry
Small molecule technologies	Various fields	 Synthesis, characterization, modification/functionalization, and assembly of small molecules Characterization (DNA binding, 	 Control or detection of gene expression Recognition of DNA sequences Detection of cell interaction, energy control Cell therapy Blocking of fat synthesis
Terahertz technologies			Development of high-power THz wave generation technique
Water		Study of THz water dynamics, thin films	
MOF/PCPs, solar cells, perovoskites,		 Synthesis, characterization, modification/functionalization, and assembly of synthetized materials (gas selectivity, 	 Development of devices and systems (gas separation, hydrogen storage, catalysis, luminescent sensing, etc.)
Drug delivery systems	Basic understanding of biological processes	 Development and characterization of drug and gene carriers 	 Drug delivery systems (chemotherapy, gene therapy, cell engineering, etc.)
Cancer	 Signaling networks Regulation of gene expression Basic understanding of cancer 		
Heart	 Theory of the heart: biomechanics, biophysics, and nonlinear dynamics of cardiac function 		Therapies for cardiac arrythmias
RNA imaging			
Single-molecule imaging	 Elucidation of the way biomolecules operate (proteins, nucleic acids) Understanding of membrane mechanisms DNA conformation 		 Single-molecule tracking techs Single-molecule observation/imaging
Microfluidics		 Approaches, methods and components that can be incorporated into microfluidic devices, e.g.: degassing approaches, 	 Development of devices and systems (high-throughput systems, single cell arrays, etc.)

Supplementary Tables 2 Biserial correlation matrices

a) Wyss Institute

Correlations			\square	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
															2	ы																		
				MON	TIVE_MATS		E_EDITING	OFLUID_DEV	LINEAR	OTS	rdev	THBIOL	UE_BIOMAT	UE_CARDIO	UE_DRUGDE	UE_MECHAN	MP	g	ш	Ŧ	٢S		NTRY	HOR	CAL		PANY	MPANY	PITAL	SPITAL	ACTOR	TATION	C_RAO	C_ENTROPY
	WERAGE	STD DEV		IATUR_K	CLU_ADAF	SLU_DNA	CLU_GENE	CLU_MICR		CLU_ROB(ITU_SOFT	INVR	CLU_TISSI	CLU_TISSI	SLU_TISSI	SLU_TISSI	IELD_COI	IELD_ENG	וברם_נוד	IELD_MA	IELD_PHY	EAR	um_cou		ERC_LOC	UM_PIS	IUM_CON	ERC_COI	NUM_HOS	ERC_HO	MPACT_F.	IORM_CIT	NTERDISC	NTERDISC
1 NATUR_KNOW	2.145	0.739	716	1	0	- 0	0	- 0	- 0	0	0	0	0		0	0	u.	<u> </u>	<u>u</u>	<u> </u>	<u>u</u>	~	~	~	<u>u</u>	~	~	<u> </u>	~	<u>u</u>	=	~	=	
2 CLU_ADAPTIVE_MATS	0.074	0.262	716	.013	1																													
3 CLU_DNA	0.045	0.207	716	061	086	1							<u> </u>											_									-+	
4 CLU_GENE_EDITING	0.064	0.245	716	194	078	069	1																										-+	
5 CLU_MICROFLUID_DEV	0.070	0.255	716	.198"	079	070	063	1																										
6 CLU_NONLINEAR	0.071	0.257	716	049	089	079	071	072	1																									
7 CLU_ROBOTS	0.049	0.216	716	.153	078	069	062	063	071	1																								
8 CLU_SOFTDEV	0.133	0.339	716	.201	101	090	081	082	093	081	1																							
9 CLU_SYNTHBIOL	0.177	0.382	716		119	106	095	097	109"	095	124	1																						
10 CLU_TISSUE_BIOMAT	0.073	0.260	716	.027	128	114"	103	104	118	103	134	158	1																					
11 CLU_TISSUE_CARDIO	0.066	0.248	716		065	058	052	053	060	052	068	080	086	1																				
12 CLU_TISSUE_DRUGDELIV	0.089	0.285	716		096	085	077	078	088	077	100	118	127"	064	1																			
13 CLU_TISSUE_MECHANOT	0.080	0.271	716	147	075	067	060	061	069	060	078	092	099	050	074	1																		
14 FIELD_COMP	0.008	0.032	715	.055	072	031	048	053	.087	.284	.027	021	099"	.044	058	057	1																	
15 FIELD_ENG	0.083	0.139	715	.243	122		145	027	019	.424	.234	215	.126	021	076	071	.380	1																
16 FIELD_LIFE	0.531	0.352	715	226	345	140	.285	062	.033	103	305	.418	201	.156	.159	.166	112	379"	1															
17 FIELD_MATH	0.011	0.032	715		098	009	.012	087	.288	.035	094	.098"		.032	068	020	.235	017	.098	1														
18 FIELD_PHYS	0.366	0.334	715	.145"	.431	.214"	236"	.090*	062		.230		.181"				159	052		214	1													
19 YEAR	2012.5	1.4	716	.057	048	031	.018	054	.018	.058	.098	042	.080	048		042	.061	.149"	163"	.019	.102	1												
20 NUM_COUNTRY	1.513	0.881	716	.062	063	124	111"	.167	046	051	064	084		066	038	007	062	014		086			1											
21 NUM_AUTHOR	6.750	4.239	716	024	053	071	009	.044	109	098	030	.119	.096	.007	.056	.014	092	104	.128	.011	083	.116	.244	1										
22 PERC_LOCAL	0.783	0.295	716	022	.103	.066	.109"	080	.004	.027	.108	.034		.077	049	.071	.006	.008	.035	052	036	088	450	251	1									
23 NUM_PIS	1.219	0.503	716	.174"	.031	002	085	005	.002	.033	.124	.100"	141"	078	006	.079	.029	.138"	.002	.010	063	.048	134	.092	.188	1								
24 NUM_COMPANY	0.046	0.229	716	.076	063	008	.028	.000	058	.028	024	.070	083	012	.155	022	011	043	.126	.029	117"	113	062	.157	165	.058	1							
25 PERC_COMPANY	0.014	0.084	716	.103"	051	032	.039	.009	047	.024	038	.022	068	031	.204"	033	013	050	.102	.011	086	132"	072	.112"	165	.052	.756"	1						
26 NUM_HOSPITAL	0.529	0.825	716	.025	182	.020	132	.109	.015	031	122	.060	.157	067	.061	.115	078	086		034	199	028	.183	.430	086	.024	011	024	1					
27 PERC_HOSPITAL	0.204	0.314	716	.068	177"	.055	150	.197"	.020	048	168	083	.284"	086	012	.186	076	056	.130	040	102"	070	.182"	.167"	.032	041	053	055	.712"	1				
28 IMPACT_FACTOR	10.899	10.235	701	076	.042	.151"	.198	062	074	105"	047	.161"	085	040	064	022	026	195"	.070	.019	.004	103	094	.137"	.075	.108"	.001	018	.023	039	1			
29 NORM_CITATION	3.561	5.537	715	.013	.008	.039	.289	004	098	092	.024	026	.016	016	074	.014	033	081	.009	026	.030	008	027	.078	.091	.011	022	045	.016	010	.442	1		
30 INTERDISC_RAO	0.447	0.143	714	.346"	107	023	279"	.156	.119"	.237"	.093	414"	.164"	.068	.111"	087	.193	.397"	280"	.042		.057	.030	040	021	.123	.023	.028	.012	.086	269	141"	1	
31 INTERDISC_ENTROPY	2.097	0.345	714	.233	044	087	192	.166	058	.015	.041	276	.212	.103	.177	016	.018	.084	218	011	.195	.021	.084	.038	.001	.070	.005	.014	.022	.089	121	.000	.682	1

**. Correlation is significant at the 0.01 level (2-tailed) *. Correlation is significant at the 0.05 level (2-tailed).

b) WPI-iCeMS



**. Correlation is significant at the 0.01 level (2-tailed) *. Correlation is significant at the 0.05 level (2-tailed).

NOTES:

- Results are based on 2-tailed Pearson's biserial correlations.
- Abbreviations → NATUR_KNOW: Cognitive contents; FIELD_COMP: computer sciences; FIELD_ENG: engineering; FIELD_MATH: mathematical sciences; FIELD_PHYS: physical sciences; YEAR: publication year; NUM_COUNTRY: number of countries; NUM_AUTHOR: number of co-authors; PERC_LOCAL: percentage of local collaborators; NUM_PIS: number of PIs; NUM_COMPANY: number of firms as co-authors; PERC_COMPANY: percentage of co-authors from companies; NUM_HOSPITAL: number of hospitals as co-authors; PERC_HOSPITAL: percentage of co-authors from hospitals; IMPACT_FACTOR: normalized impact factors; NORM_CITATION: normalized citation; INTERDISC_RAO: Rao-Stirling diversity index; INTERDISC_ENTROPY: entropy index.
- CLU variables refer to the research fronts listed in the tables of Fig. 6.