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The manifestos from Dagstuhl Perspectives Workshops are published in the *Dagstuhl Manifestos* journal. Each manifesto aims for describing the state-of-the-art in a field along with its shortcomings and strengths. Based on this, position statements and perspectives for the future are illustrated. A manifesto typically has a less technical character; instead it provides guidelines and roadmaps for a sustainable organisation of future progress.

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— Abstract -

The study of learning in adversarial environments is an emerging discipline at the juncture between machine learning and computer security. The interest in learning-based methods for security- and system-design applications comes from the high degree of complexity of phenomena underlying the security and reliability of computer systems. As it becomes increasingly difficult to reach the desired properties solely using statically designed mechanisms, learning methods are being used more and more to obtain a better understanding of various data collected from these complex systems. However, learning approaches can be evaded by adversaries, who change their behavior in response to the learning methods. To-date, there has been limited research into learning techniques that are resilient to attacks with provable robustness guarantees

The Perspectives Workshop, "Machine Learning Methods for Computer Security" was convened to bring together interested researchers from both the computer security and machine learning communities to discuss techniques, challenges, and future research directions for secure learning and learning-based security applications. As a result of the twenty-two invited presentations, workgroup sessions and informal discussion, several priority areas of research were identified. The open problems identified in the field ranged from traditional applications of machine learning in security, such as attack detection and analysis of malicious software, to methodological issues related to secure learning, especially the development of new formal approaches with provable security guarantees. Finally a number of other potential applications were pinpointed outside of the traditional scope of computer security in which security issues may also arise in connection with data-driven methods. Examples of such applications are social media spam, plagiarism detection, authorship identification, copyright enforcement, computer vision (particularly in the context of biometrics), and sentiment analysis.

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1 Executive Summary

Anthony D. Joseph, Pavel Laskov, Blaine Nelson, Fabio Roli, and J. Doug Tygar

Arising organically from a variety of independent research projects in both computer security and machine learning, the topic of secure learning is emerging as a major direction of research that offers new challenges to both communities. Learning-based approaches are particularly advantageous for security applications designed to counter sophisticated and evolving adversaries because learning methods can cope with large amounts of evolving and complex data. However, the assets of learning can also potentially be subverted by malicious manipulation of data. This exposes applications that use learning techniques to a new type of security vulnerability in which an adversary can attempt to evade learning-based methods. Unlike many other application domains of machine learning, security-related applications require careful consideration of their adversarial nature and novel learning methods with improved robustness against potential attacks. The Perspectives Workshop, "Machine Learning Methods for Computer Security", brought together prominent researchers from the computer security and machine learning communities interested in advancing the state-of-the-art in the field of secure learning, discussing open problems, and promoting further collaboration between the two communities.

This workshop focused on tasks in three main topics: the role of learning in computer security applications, the paradigm of secure learning, and the future applications for secure learning. These themes arose throughout the majority of plenary presentations and were the subjects of focused discussions within separate working groups. In the first group, participants discussed the current usage of learning approaches by security practitioners. The main conclusion of their discussion was that there is a pressing need for a tighter integration of machine learning methods into the operational practice of security systems to enable improved response and proactive functionality. The second group focused on the current approaches and methodical challenges for learning in security-sensitive adversarial domains. The key open problem identified in this area was a want for a formal notion of security for data-driven applications, similar to that used in classical information security, and for the development of learning algorithms with provable security guarantees. Finally, the third group addressed future application domains that would benefit from secure-learning technologies. It is to be expected that the demand for secure data analysis will expand into new application domains whenever attackers discover new opportunities for monetary profit by abusing deployed data-driven technologies.

Several themes arose recurrently during the workshop. One of the major concerns discussed was the reluctance of security practitioners to use learning-based techniques due to their opacity. To address this problem, new learning methods should be developed with higher transparency and interpretability. Further, the issue of incorporating human operators into the learning process to prevent unintended consequences was identified as an important research direction. Finally, benchmarks for and quantitative assessments of the security of learning algorithms were also deemed to be currently inadequate.

Yet the most important outcome of this workshop is the new found sense of an emerging scientific community growing at the junction of computer security and machine learning. Even though the scientific traditions and practices of machine learning and computer security diverge in many aspects, regular scientific exchange is indispensable in this field and should be promoted with joint projects, professional networks and dissemination activities.

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2 Introduction

Anthony D. Joseph, Pavel Laskov, Blaine Nelson, Fabio Roli, and J. Doug Tygar

The emergence of the Internet has revolutionized modern society. It has changed the way we do business, manage our personal lives and communicate with our friends. To a large extent, the Internet owes its success to the enormous amount of data it generates and to novel decision-making instruments based on data analysis. Online advertisement, recommendation systems, consumer profiling, and many other Internet-related businesses crucially depend on data analysis and the underlying methods of machine learning, which extract meaningful information from seemingly unstructured masses of data.

Unfortunately, the ubiquity of the Internet has also stimulated its abuse and the rise of sophisticated cyber-crimes. It has enabled criminals to build sustainable businesses that rely on the exploitation of security vulnerabilities. To avoid being detected by security mechanisms, the attackers develop new exploitation techniques; an act which places tremendous pressure on cybersecurity vendors. To speed up development of adequate defenses, the latter are forced to resort to data-analysis techniques to extract information from prodigious amounts of security data. The vendors' successes, in turn, motivates the attackers to develop new tricks to evade detection.

The cat-and-mouse game between the security industry and the cyber-criminal underground points out a fundamental scientific problem associated with data analysis and machine learning techniques: they were originally conceived under the assumption of "faithful" data and did not explicitly account for potential data manipulation by adversaries. Several studies have shown that data-driven security instruments can be easily broken [44, 96], which raises the question of whether machine learning methods can be deployed at all in adversarial environments [10].

Recent developments in the learning methodology, *e.g.*, [20, 37, 60], and the growing experience with its application in the security practice, *e.g.*, [31, 70, 100], have underlined the necessity for deeper understanding of the security aspects of machine learning. These developments have motivated the Perspectives Workshop "Machine Learning Methods for Computer Security" held at Schloss Dagstuhl from the ninth to the fourteenth of September, 2012. Presentations and discussions held during this workshop were aimed at producing assessments of the state-of-the-art methodologies and at identifying open problems and research priorities. The workshop was also a major step in molding the scientific community in this emerging field of secure machine learning. It has brought together researchers from various disciplines ranging from machine learning and security to spam filtering, online advertisement and computer forensics. This manifesto summarizes the key findings of the workshop and provides an overview of the future scientific developments in secure machine learning.

The following three themes can be seen as the cornerstones of the workshop's discussions and of the results presented in this manifesto:

- 1. Machine learning for security. What security problems can machine learning best help to solve? What scenarios are they ill-suited for? These and many other scientific and operational issues are discussed in Section 3.
- 2. Secure machine learning. What are the theoretical limitations of worst-case attacks against learning algorithms under different constraints? How can these constraints

be used in practice for protecting learning methods against adversarial data? These methodological issues are discussed in Section 4.

3. Secure learning beyond security. What are existing and emerging non-security applications where learning techniques are used and can potentially be exposed to adversarial data? What experience from these applications can be used for development of general methodology of secure learning? These issues are discussed in Section 5.

Finally, it must be noted that most of security-related decisions involve a human operator. As such, humans are often the first targets of attacks using "social engineering" tricks such as deception or impersonation. Although consideration of the social factors associated with security was outside of this workshop's scope and beyond the expertise of its participants, the need to address the social dimension of security and to integrate data-analysis tools with human decision-making capabilities was consistently re-iterated during the workshop.

3 Machine Learning for Computer Security

Battista Biggio and Nedim Šrndić

The rapid development of security exploits in recent years has fueled a strong interest in data analysis tools for computer security. On the one hand, the sheer number of novel malicious software observed by security researchers transcends the limits of manual analysis.

According to AVTEST,¹ more than 200,000 examples of new malware are sighted daily [5]. However, most of these instances represent only minor variants of existing malware strains. Nonetheless, correctly identifying the specific strain of a given malware sample requires sophisticated classification methods beyond hashes, simple rules, or heuristic fingerprints. Beyond simple malware polymorphisms and obfuscations, the increasing professionalization of the "attack industry" leads to particularly hard cases in which genuinely novel exploitation techniques are employed. Conventional methods based on hashes, signatures, or heuristic rules cannot deal with such threats in a timely fashion. Anomaly-based detection methods appear to be the best alternative for such cases, even if they inevitably cause some false positives.

Historically, the development of machine learning and computer security has been reciprocal. The early work on intrusion detection, starting from the seminal paper of Denning [38], formulated intrusion detection as a data analysis problem in which a decision function is based on a model automatically derived from previous benign examples. Stemming from both the security and machine learning communities, followed this anomaly-based approach [45, 69, 71, 126]. Additional machine learning techniques such as supervised classification and clustering have also proved to be useful to various security problems [11, 99, 122]. Certain characteristics of security problems are atypical for classical learning methods and require the development of customized techniques. These characteristics include strongly unbalanced data (attacks are very rare), unbalanced risk factors (low false positive rates are crucial), difficulties in obtaining labeled data, and several others.

¹ http://www.av-test.org/en/home/

The most crucial peculiarity of security as an application field for machine learning is adversarial data manipulation. All security technologies are sooner or later subjected to attacks. Hence, the analysis of potential attacks is a fundamental aspect of security research. Consideration for adversarial data is not addressed by classical machine learning methods, which has hindered their acceptance in security practices. Recent developments in both fields have brought a significant understanding of the general factors that affect the security of learning algorithms. The remainder of this chapter provides an overview of the state-of-the-art work, open problems and potential applications for the learning-based security technologies.

3.1 State-of-the-art

A classical security application of machine learning is detection of malicious activity in operating systems data or network traffic: "intrusion detection systems". A substantial amount of work in intrusion detection followed various learning-based approaches, in particular, anomaly detection [45, 69, 71, 126], rule inference [72, 73, 74, 78] and supervised learning [87, 88]. Although most of the proposed methods performed well in controlled experiments, most of the practical intrusion detection systems, such as Snort [104] and Bro [95], are still rooted in the more conservative signature-based approach. Sommer and Paxson discussed several practical difficulties faced by learning-based intrusion detection systems [112]. Among the key challenges they identified are the high cost of classification errors, the semantic gap between detection results and operational interpretation, the enormous variability and non-stationarity of benign traffic, as well as the difficulty to perform a sound evaluation of such systems.

A key lesson to be learned from the limited use of learning-based methods in the general intrusion detection context is the necessity for a precise focus on the semantics of specific applications. Several narrowly focused systems developed in the recent years have demonstrated that, in certain applications, learning-based systems significantly outperform conventional approaches depending on expert knowledge. One of the most successful application domains for such narrowly focused systems is web application security. Due to the extreme versatility of web applications, it is next to impossible to devise signatures for specific attack patterns. The learning systems overcome this difficulty by automatically inferring models of benign application-specific traffic. Such models can be used to detect malicious web queries [39, 51, 64, 113], to detect logical state violations in web applications [30], and even to develop reactive mechanisms such as reverse proxies [123] or the sanitization of web queries [66].

Another crucial contribution of learning-based systems lies in the realm of dynamic malware analysis. To stay abreast of the recent trends in malware development, most anti-virus vendors deploy sophisticated systems to acquire novel malware. Such systems have been very successful in collecting masses of data, resulting in an urgent need for tools to automatically analyze novel malware. One of the first methods for malware analysis based on reports from its execution in a sandbox used hierarchical clustering to infer groups of related malware [6]. An alternative approach based on supervised learning enabled classification of malware into known families as well as detection of novel malware strains [99]. Subsequent research has improved scalability of the above mentioned methods and verified their feasibility for large-scale malware attribution [11, 102, 122].

A similar synergy between machine learning and malware analysis has been exploited for automatic signature generation (ASG). Early ad-hoc ASG systems combined extraction of

string tokens with frequency analysis, which roughly corresponds to the idea of naive Bayes learning [57, 93]. The key weakness of such methods was their susceptibility to attacks, which made it possible to evade a deployed system or increase its false alarm rate [94, 96]. Even though this difficulty is intrinsic to all methods based on string tokens [114, 124], the ASG methods proved to be very useful for several related problems, including the detection of botnet communications [101] and network protocol reverse engineering [27, 33] that are less prone to adversarial data.

The recent emergence of JavaScript-based exploitation schemes such as drive-by-downloads and malicious non-executable files raises a number of new challenges for detecting such threats. The effectiveness of these attacks is due to their ease of deployment and distribution (*e.g.*, via malicious web sites or targeted email messages) as well as to almost unlimited options for obfuscation. Detection of such threats is further complicated by the need to understand the syntactic context of malicious content. But these problems have largely yielded to learning-based approaches built on appropriate features. Static analysis of JavaScript token sequences has been successfully deployed for detection of drive-by-downloads [100] and JavaScript-bearing malicious PDF documents [70]. Another form of static analysis with a focus on PDF document structure was instrumental in recently developed highly effective methods for detection of PDF malware [80, 111, 115]. Dynamic analysis of JavaScript string allocations combined with classification of string payloads has been successfully used for in-browser detection of drive-by-downloads [34].

To summarize, machine learning methods are currently widely used as a component in general reactive security architectures. They can optimally address targeted data-related security problems with clear semantics and well-defined scope. A key advantage of learningbased approaches is their ability to generalize information contained in data, even though such generalization may not be easily expressible in a human-readable form. At the extreme, the generalization ability of learning methods can even enable detection of previously unseen zero-day attacks.

A crucial factor for the success of learning methods in security problems is a careful design of features, which incorporate the semantics of respective applications. While yielding excellent detection rates, learning methods occasionally may result in false alarms which can, however, be mitigated through appropriate tuning of detection thresholds. Another part of the "operational price" of learning-based approaches is the black-box nature of their predictions: even in the case when highly accurate detection is feasible, it is not always possible to identify the specific set of features that were "responsible" for these predictions. This limitation must be taken into account in their operational deployment.

3.2 Open Issues and Research Directions

A number of open issues and future directions arise in the field of machine learning for computer security. Investigation of these will enable tighter integration of machine learning into the operational practice of security systems, enable an improved response and facilitate proactive efforts through early discovery of security flaws and vulnerabilities.

3.2.1 Integration of machine learning with security mechanisms

Given the proven success of learning-based approaches to narrowly focused security tasks, it is natural to expect that tight integration with existing security instruments may deliver substantial qualitative benefits for the latter. However, such integration is by no means a

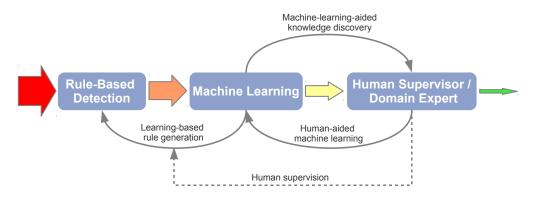


Figure 1 The abstract architecture of reactive security mechanisms utilizing machine learning.

simple task. Figure 1 shows the abstract architecture of learning-enhanced reactive security mechanisms.

The vast majority of security-related data can be handled using simple rule-based detection methods. Rules operate quickly, cheaply and accurately, and they are simple for the domain experts to understand and maintain. However, rules are not powerful enough to handle cleverly crafted and novel input samples. Although they represent only a small fraction of the total input samples, such samples may inflict substantial damage if not stopped. Machine learning algorithms can play a pivotal role here by potentially detecting completely novel, previously unseen attack samples. By providing confidence intervals for their predictions, learning methods can prioritize data to be manually inspected by experts and thus largely improve the productivity of these analysts.

To improve the feedback between the individual components presented in Figure 1, a number of open problems must be investigated:

- Learning-based rule generation. Although rule-inference algorithms are well-known in machine learning (e.g., C4.5 [98] or RIPPER [26]), they are prone to overfitting and can be easily evaded by an adversary. Novel rule inference methods are needed that are able to produce concise interpretable rules, detect anomalous events in the absence of label information and deal with adversarial data. An example for advanced rule-oriented learning is automatic discovery of regular expression patterns for spam detection [97].
- Human-aided machine learning. The supervisory role of security experts is essential for the success of learning methods in this domain. However, security expertise does not fit into traditional binary or multiclass categories common for classical learning methods. In order to learn models with high predictive power, new techniques for interaction between the learning methods and the security experts need to be investigated.
- Machine-learning-aided knowledge discovery. Security analyst's work can also be greatly faciltated by applying appropriate learning techniques. For example, active learning techniques may be deployed to suggest interesting data for a detailed investigation [2, 67, 85]. Such approaches may be especially beneficial for security applications in which manual analysis is very time-consuming and requires profound expertise.

Operational deployment of learning methods is always an iterative process. Changes in data patterns (distributional shift) makes periodic re-training of learning system is a necessary practice.Further investigation is required to understand the impact of such non-stationarity on the learning-enhanced reactive security architecture described above.

3.2.2 Reactive approaches

Machine learning for security has been primarily used for detection of malicious activity. Yet the potential high cost of security violations calls for countermeasures that can be initiated automatically. Only limited work has addressed such methods so far, *e.g.*, [65, 66, 123]. The main challenge for reactive approaches is to develop mechanisms for measuring the risk of automatic decisions which is critical for the widespread utilization of these decision-making techniques in practical security applications.

3.2.3 Machine learning for offensive security

The term "offensive security" refers to methods for empirical security verification of various applications. It comprises the areas of penetration testing, vulnerability research, and various fields of cryptanalytic research. Current methods of offensive security are almost exclusively based on human expertise. The existing automation tools are essentially brute force methods of various kinds: password, key and hash function guessing as well as protocol and document fuzzing. Some recent work in assisted discovery of vulnerabilities in source code has demonstrated the ability of learning methods to extrapolate knowledge about known security flaws [129, 130]. Future research should address methods for data-driven syntactic and semantic analysis of applications and detection of undesirable system states.

3.3 Future Applications

The open research problems presented in the previous section provide the ground for a wide range of novel applications in the area of security. In the following, we briefly discuss several such applications that address recent security problems and establish a bridge between academic work and practical solutions.

- Detection of advanced persistent threats. The notion of "advanced persistent threats" (APT) refers to customized malware, exemplified by the Stuxnet [120], MiniDuke [54] and Flame [119], used for espionage or cyber-warfare. The goal of such malware is to penetrate highly sensitive sites and, in some cases, to remain undetected for a substantial time period. They typically rely on novel penetration vectors (*e.g.*, zero-day exploits) and deploy extensive obfuscation techniques. Signature-based security tools are ill-suited for advanced persistent threats since they rely on previously crafted detection patterns that are too slow for targeted attacks. Machine learning methods may be better at detecting of APTs by automatically spotting anomalous events.
- Protection of mobile devices. Private and sensitive data stored on mobile devices is becoming an increasingly attractive target for attackers. Mobile devices have limited resources, and common security approaches, such as matching files against signatures, can not be applied on a regular basis. Learning methods may support mobile security by enabling lightweight and signature-independent mechanisms for detecting malicious activity, for example, by identifying unusual information leakage from a device.
- Dynamic and continuous authentication. User authentication is typically based on secrets that can be forgotten and stolen. Authentication normally is only done once, at the beginning of a session, and grants full access rights to a given identity. We envision a more flexible authentication scheme, which is potentially less prone to lost or broken secrets, using information stored about users on systems they log into. Machine learning can use stored data to learn the behavior of legitimate users. Then, in some cases, users could authenticate simply by means of their usual actions, thus reducing the

need for or bolstering traditional password-based authentication. Machine learning could strengthen passwords with questions derived from previous user activities (*e.g.*, by inferring which acquaintances the user should reasonably be able to recognize based on their web-browsing). It similarly could also be used to generate secret questions for resetting forgotten passwords. Finally, it could provide for continuous and incremental authentication during the course of a session based on comparing users activities with their profiles when users request additional privileges.

- Assisted malware analysis. Countering malicious software is a continual arms race. More often than not, there is a significant delay between the appearance of a new malware and the availability of a malware signature. A significant amount of time during development of such signatures is devoted to analyzing and understanding the inner workings of malicious programs. Machine learning methods could accelerate this process. Techniques for feature selection and visualization could be applied to emphasize patterns within a malware's code or behaviors, and thus, these techniques could facilitate the rapid development of detection patterns.
- Computer forensics. Forensics is one of the most data-intensive areas of computer security. Here, significant benefits can also be expected from applying machine learning to evaluate data of forensic images, system logs or logged network traffic in the aftermath of a security incident. In a related field of criminal forensic investigation, similar methods can be applied to identify evidence of human crimes. In both cases, the objective of learning methods should be to help focus investigator's attention on important information related to goals of investigation and, possibly, to other similar cases, by sifting through large volumes of forensic data and prioritizing the information.

4 Secure Learning: Theory and Methods

Daniel Lowd and Rachel Greenstadt

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While machine learning is a powerful tool for data analysis and processing, traditional machine learning methods were not designed to operate in the presence of adversaries. They are based on statistical assumptions about the distribution of the input data, and they rely on training data derived from the input data to construct models for analyses. Adversaries may exploit these characteristics to disrupt analytics, cause analytics to fail, or engage in malicious activities that fail to be detected. Several examples of attacks against learning algorithms have been proposed in the recent years. Some of them have been designed for specific variants of learning algorithms deployed in security applications [44, 96], others target the popular general-purpose learning algorithms [17, 61]. Such attacks exploit the adaptive aspects of a machine learning system by designing training data that will cause the learning system to produce models that misidentify future inputs. If users detect the failure, then the risks can be even greater.

The growing concern about the security of learning-based applications arises from the lack of understanding about how well machine learning performs under adversarial conditions. When a learning algorithm performs well in adversarial conditions, we say that it is an algorithm for secure learning. This raises a natural question: how do we characterize the quality of a learning system and determine whether it satisfies the requirements for secure

learning? Hence arises the need for a formal definition of the security of a machine learning algorithm; a definition that, until now, has not been fully expressed in a general context. A formal notion of secure learning would provide a means for practitioners to use learning algorithms with an understanding of their security guarantees and the conditions required for these guarantees to hold. Moreover, such a formal notion of security would encourage learning theorists to explore security properties of learning methods and, hence, would provide motivation for designing new algorithms suitable for adversarial environments. Coupled with appropriate advances in experimental methodology, the understanding of security aspects of machine learning methods would strongly increase their applicability to untrusted data and provide a quantitative assessment of the risks associated with such data.

4.1 State-of-the-art

Early theoretical work revealed that learning algorithms exhibit different behavior under adversarial noise, depending on the part of the data controlled by an attacker. In the setting of supervised classification (*i.e.*, assigning one of the two *a-priori* defined classes to new data based on prior examples of such assignments), learning algorithms can be surprisingly tolerant to wrong labels assigned by an attacker during training. Angluin and Laird [3] showed that for some classes of Boolean functions, an attacker must flip the labels of nearly half of the training data to cause the incorrect classification of selected data points. On the other hand, by controlling attributes of the data, an attacker can construct inherently difficult learning problems, in which the error rate can be nearly as high as the fraction of data under the attacker's control [56]. These contrasting results emphasize the need for clear assumptions on the adversarial power.

Empirical evidence of attacks against learning algorithms arose in the last decade in the fields of intrusion detection and spam classification where learning methods were actively used since the late 1990s. Evasion attacks against anomaly-based intrusion detection systems (IDS) have demonstrated two main evasion strategies: *poisoning*, *i.e.*, erosion of a model of normality [121], and *mimicry*, *i.e.*, insertion of a normal content into the target data [125]. Another interesting example of an attack is the *polymorphic blending* technique, a transformation of packet payload to match a certain histogram of byte occurrences [44]. Although finding an optimal blending for byte sequences of length greater than one was shown to be NP-complete, greedy approximation algorithms can significantly decrease detection rates of an IDS [43]. Highly effective attacks have also been proposed against classification algorithms. The *red herring* and *correlated outlier* attacks against automatic signature generation systems were shown to decrease their detection accuracy to an unacceptably low level of 20–30% [94, 96]. Attacks against spam filters used similar techniques to manipulate features derived from word frequencies in email messages [77, 128].

Alongside the "destructive" work summarized above, some progress has been made in the development of learning algorithms with robustness to worst-case noise. Two groups of methods should be noted here. The min-max approach (*i.e.*, training a classifier with best performance under the worst noise) results in a relatively easy optimization problem [37, 47]. The more complex game-theoretic approach is advantageous when the learner and the attacker have different cost functions; *e.g.*, the learner is trying to minimize the spam frequency while the attacker is boosting the attractiveness of spam content. Such problems can be solved using the Nash equilibrium approach, which, however, is tractable only under some stringent assumptions [19, 21]. Compared to the baseline learning algorithms, these advanced methods improve accuracy by 10–15%, which is far from a strong claim of security.

An important milestone in the study of security of machine learning was the taxonomy of attacks against learning algorithms introduced by Barreno *et al.*, 2006 [10]. This work was the first to connect security of learning with the classical objectives of information security. However, the interpretation of such connection in this work is only qualitative. Increasing the detection error of a learner is categorized as an *integrity* attack and raising the false alarm rate is defined as a threat to learner's *availability*. Such qualitative associations do not provide a means to formalize the connection to the classical security objectives.

Recent work on the security of machine learning has provided more evidence of potential attacks but yielded little insight into how they can be prevented. It has been shown that complex learning algorithms such as Support Vector Machines can also be evaded with modest evasion effort [17]. Even if the attacker has no specific knowledge about a deployed model, evasion may still be successful if the attacker can query it at run-time. Nelson *et al.* [92] demonstrated that a large group of classifiers with convex decision functions (*i.e.*, classifiers that induce a convex positive/negative class) can be evaded under such assumptions, albeit potentially at a cost of an exponential number of queries, for some cost functions.

In summary, the most progress in the study of security of machine learning has been made in identifying the security weaknesses of learning methods. While there exist methods with improved robustness against attacks, such improvements are insufficient to claim strong security. Very little attention has been given so far to the investigation of autonomous learning methods, apart from the online anomaly detection studied by [60, 61]. Finally, the limited existing methodology for security analysis, thus far, has not provided results that have improved the design of novel learning algorithms.

4.2 Open Issues and Research Directions

4.2.1 Formalization of Secure Learning

Formalisms in both the security and machine learning (ML) communities (for example, cryptographic security, Byzantine fault tolerance, probably approximately-correct learning, and empirical risk minimization techniques) have catalyzed research in their respective fields and led to major advances in both theory and practice. Formalisms for secure ML have the potential to do the same.

Ideally, security metrics for ML systems will provide:

- A mechanism for inter-algorithm comparison,
- The ability to provide strong performance guarantees, and
- A mechanism for determining whether an algorithm is appropriate for use in a particular security setting.

However, there need not be a single metric or framework that captures all aspects of security. Different metrics might be best-suited for different tasks or for different aspects of the evaluation.

There are several frameworks for secure learning that form a foundation for secure learning. The qualitative taxonomy of security threats to learning techniques defined by Barreno *et al.* [9] provides a coarse granularity for separating different threats, many of which may require very different notions of a security measure. Within this augmented taxonomy, metrics for algorithmic security have emerged in two distinct areas: near-optimal evasion for exploratory attacks against learners [76, 92], and differential privacy for privacy exploratory attacks against a learned model [40].

There is a general need for a metric for causative attacks, S, that evaluates the (worstcase) effect of an attack scenario, in which the attacker is able to manipulate the training data to mislead the learning algorithm. This particular portion of the attack taxonomy of Barreno *et al.* has been explored in prior work, but remains without a clear definition of security required of the learner. Such a measure should incorporate some notion of stability under adversarial contamination and also must incorporate limits on the adversary's effect on the learned model in order to model tractable threats. Thus, this measure can be considered as a function, $S(L, A, \epsilon)$, expressed in terms of the type of learner, L, the model of the adversary and his available actions, A, and the power or total resources allocated to the adversary (such as fraction of training examples he controls), ϵ .

Another promising direction is to define new **security-aware loss functions** that can be directly minimized by ML algorithms. Such functions would measure the "damage" done to the estimator under the non-stationarity introduced by the adversary's contamination. Thus, this loss would necessarily be specific to the algorithm and the learning setting.

In some cases, these metrics may provide theoretical guarantees about the security or vulnerabilities of a particular method, as in differential privacy or minimal-cost evasion. Many of these metrics can also be used empirically (as in Section 4.2.2) to assess how a particular algorithm behaves under this security metric for the specified adversarial model.

4.2.2 Empirical Evaluation

Current empirical techniques for performance evaluation of machine learning algorithms (*e.g.*, hold-out and cross-validation techniques), as well as performance metrics (*e.g.*, accuracy), do not take into account adversarial settings; *i.e.*, adversarial manipulation of training and/or testing data distribution with respect to data collected for classifier design. Therefore, such techniques can not provide information about the security of a classification system under attack, and are likely to provide over-optimistic estimates of their performance [9, 22, 23, 62, 68]. Besides theoretical analyses of the security of machine learning algorithms, it is thus necessary to develop methods for empirically evaluating, on a given set of data, the security of classifier design (including the feature selection/extraction and model selection steps) and for deployed classification systems. Such methods will be useful for researchers, and also for practitioners, and it is desirable that they are implemented in ad hoc software tools.

Unlike the traditional performance evaluation, which relies on the stationarity assumption about data distribution, security evaluation would be better approached as a *what-if* scenario analysis which is well known in other fields [103]. Any attack scenario implies that training and testing datasets follow different distributions. It is not possible to know in advance what kinds of attacks a given learning algorithm or classifier system will be subject to, as well as their characteristics (*e.g.*, adversary's knowledge and capability). Security evaluation should then be performed against several possible attacks and for different characteristics of each attack under which it can be of interest to assess the behavior of the considered algorithm or systems, chosen according to the task at hand.

4.2.3 Development of Secure Learning Approaches

Most current applications of machine learning to security problems use standard machine learning algorithms, which do not explicitly model an adversary. As the adversary adapts, humans respond by retraining the model with new data, as well as by manually inventing new features when necessary. More research is needed to understand when this "vanilla" approach is sufficient, or even superior to more complex approaches that incorporate adversarial reasoning. Another important direction is to develop generic approaches to making machine

learning algorithms secure, rather than manually developing a separate adaptation for each algorithm. A wrapper that guaranteed security would allow any algorithm to be made secure, allowing secure machine learning to take advantage of the latest advances in standard machine learning; thereby separating the learning and security elements of the problem.

One of the potential methodological avenues for development of secure learning algorithms would be to explore the connection to online and non-stationary learning, which were specifically designed to deal with distributions that change over time. Modeling non-stationary processes has been a subject of an extensive body of research, and many algorithms for statistical inference, prediction and classification have been proposed [35, 50, 58]. Nonstationary problems are naturally handled in the online learning setting. The field of online learning encompasses many areas, such as online prediction in a statistical setting [48], in the regret minimization setting where information can be partial or the prediction task can be adversarial [24], as well as the general reinforcement learning problem [117]. In order to apply online learning methods to security problems, we first need to define a utility function Umapping from the joint outcome and decision space to a numerical value.² There is a crucial link between the utility function U and the security function S. In particular, it should follow that the expectation of U given a particular model and algorithm L and adversary Aequals S(L, A). This also facilitates the future evaluation of the algorithm because U can be used as an evaluation metric.

4.2.4 Data sanitization

Another potential countermeasure against adversarial noise is to identify and remove malicious data, known as *data sanitization*. Several approaches to data denoising have been explored in prior work. Zighed *et al.* [131] proposed a method to identify mislabeled samples, which was based on a statistical technique called the *cut edge weight statistic*. A sample close to another class has a higher chance to be an attack sample. Misclassified samples are treated as attack samples during the training process in [18, 52, 127]. The *Reject On Negative Impact* (RONI) defense proposed by [91] eliminates the samples which have negative impact on learning performance. Similar techniques have been proposed in the context of anomaly detection, using partitioning of the training data and cross-validation of models trained on individual partitions [32]. Although sanitization techniques proved to be successful in selected scenarios, their applicability as a general defense against adversarial noise remains to be investigated.

4.3 Secure Learning and Data Privacy

Privacy-preserving learning has been studied by research communities in security, databases, computer theory, machine learning, and statistics. More recently, the strands of this work have begun to merge, with the formalism of *differential privacy* from the theoretical computer science community being most popular [41]. This definition is intuitive and very strong in a formal sense, as it provides guarantees analogous to those provided in cryptography. A significant amount of work has already been done to understand how simple analyses can be performed while guaranteeing differential privacy and still yielding meaningful results [7, 12, 53]. However little has been done to produce differentially-private versions of the mainstream machine learning algorithms with a few exceptions including [25, 84, 106].

² In general though, we can also consider a multi-objective setting if we do not desire to select a particular utility function, a priori.

Numerous applications of machine learning, which are intended to provide societal benefits or drive private profits, operate on privacy-sensitive data. Just a few examples of such data include health records, personal communications, utility usage, online social networks, and mobile location data. As more of these services move online, and the automatic mining of such data becomes more prevalent, it is becoming increasingly necessary to establish technical approaches for protecting privacy and regulatory incentives to encourage the adoption of learning approaches.

Several well-known examples of privacy breaches in data released for statistical analysis exist, of which many have been a direct result of the application of machine learning techniques. In the 1990s, the U.S. state of Massachusetts released hospital records of state employees for the use by medical researchers, after removing names, addresses and social security numbers. However, removing these identifying features proved to be insufficient to truly preserve the privacy of this data as a researcher was able to cross-link the released data with easily obtainable state voter records containing names, addresses and postal codes, and thus, she was able to identify records with the names of several individuals [118]. The release of such data would clearly be detrimental, for example, to individuals hoping to conceal difficult treatments from family and friends or from the health insurance industry, which is often eager to obtain such information about individuals for risk assessments. Then, in 2006, AOL attempted to de-anonymize a large volume of search query logs by removing so-called personally identifying information (PII), and they released the data for use by ML researchers [8]. While such a well-intentioned act was immensely valuable for research in information retrieval and search, a journalist from the New York Times was able to identify an elderly AOL user—and her private, potentially embarrassing online habits—by linking the unique terms she queried in the log. In a third case of a company releasing data, the "anonymized" movie recommendations of Netflix users were de-anonymized by researchers by joining the data with public IMDB movie ratings having named users. This, in fact, resulted in the unwanted publication of a user's sexuality [89]. Finally, it is common knowledge that online advertisers track and construct highly specific profiles of users using machine learning, so that advertisements may better target individuals likely to make purchases. A student recently leveraged identifying attributes of users such as geographic location, workplace, and schooling history, to study advertisements with an additional private attribute of interest. Depending on whether or not the ad was shown, the student was able to determine the value of the private attribute of the user in question [63]. Such an attack on learning-based advertising could reveal political preferences, sexuality, or other sensitive personal attributes.

To avoid the increasingly frequent privacy breaches by institutions entrusted with individuals' data, a two-pronged approach of regulation and technical tools is required. It is imperative to understand the full consequences of concerted attacks on the privacy of user data, going beyond the relatively simple illustrative examples provided above. It is also important to have standardized metrics that quantify the privacy of released data. Along with formal measures must come an understanding as to whether methods that preserve data privacy provide the level of utility required for specific applications such as targeted advertisements, location-based shopping deals, medical research, *etc.* To this end, the development of privacy-preserving anonymization and statistical analysis must provide guarantees on both privacy and utility. Theoretical work should also seek negative results, *e.g.*, finding learning tasks, for which one provably can not simultaneously attain utility and privacy.

5 Future Applications of Secure Learning

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Computer security is not the only field in which attacks against the learning systems have been observed. Almost concurrently with the discovery of the first attacks against intrusion detection systems, similar methods appeared for evasion of statistical spam filters [76, 90]. Both of these application domains provided inspiration as well as experimental foundation for developments in secure learning [20, 36]. We expect that the demand for secure data analysis will grow and expand to other application domains whenever attackers discover new opportunities for monetary profit by abusing data-driven technologies. In the following sections, we present the analysis of the main factors, which may make specific application domains attractive for novel attacks against learning methods and survey the situation in several domains, in which learning technologies play a crucial role.

5.1 State-of-the-art and emerging technologies: Where do adversaries attack next?

Unlike Sections 3 and 4 where our recommendations are based on existing prior work, in most application domains beyond computer security, with the exception of email spam filtering, there is hardly any prior experience with adversarial noise. Hence we begin our survey with a focused review of the literature on spam filtering and then attempt to extrapolate this experience to other applications domains.

The key factor in the assessment of the relevance of secure learning to specific applications is the existence of a business case. As experience shows, serious security threats arise mostly when miscreants can make money by exploiting technical vulnerabilities. This was the case with classical malware that could be made profitable in a variety of different ways. Typical monetization schemes deployed by cyber-criminals include stealing login credentials, credit card numbers and bank accounts from end-users, operating networks of compromised computers (botnets), including renting them out, demanding ransom for encrypted data or to avoid denial-of-service attacks, among many others. Email spam was fueled by its potential to reach a huge population of email users with unsolicited advertisement at almost no cost; such advertisements were backed by real, albeit often illegal, businesses. The "business case" may not necessarily involve monetary profit; attack targets may also be intellectual property or classified information, as the recent cases of cyber-espionage show [81].

5.1.1 Spam filtering

Spam filtering is the most popular example of machine learning applications that has to deal with adversarial inputs. Many modern email clients have an automatic spam filtering function that partially incorporates machine learning techniques, thus proving both its scientific relevance of and the business case for this application. During the past fifteen years, machine learning techniques have been widely investigated and used to analyze the textual content of email messages. Moreover, the adversarial nature of spam filtering is apparent and can be cast into a "game" between spammers and the adaptive spam filter. For all these reasons, spam filtering has received much attention in the scientific community; *e.g.*, [13, 28, 49]. Most papers on adversarial learning use it as one of the test cases for experiments,

and it was used as a paradigmatic application in seminal papers on the modeling of adversarial learning [36, 76]. The evolution of spam filtering is also instructive for understanding the nature of an "arms race" within a typical adversarial learning application domain. Interested readers can find additional details on this evolution in the "spammer compendium"³. In early spam, the message body of spam emails consisted mostly of plain text without any explicit or malicious attempts to evade detection. But, as anti-spam filters improved, spammers have evolved from naive attempts to bypass these filters to specialized mimicry attacks that make it difficult to distinguish spam from legitimate e-mail based solely on a message body. Around 2004, spammers introduced the image-spam trick, which consists of removing the spam message from the email body and instead embedding it into an image sent as an attachment [16, 46]. This allowed spammers to bypass any sophisticated and effective analysis of email body texts. Image-based spam is a notable example of how attackers change when the defense becomes too effective. To detect image-based spam, computer vision techniques have been developed and specialized modules implementing them have been plugged into many anti-spam filters.⁴ This is also an example of defenders reacting to attacks by changing the features used for detection.

5.1.2 Advertising

Online advertising is a maturing industry with billions of dollars at stake, which opens opportunities for adversaries to leverage the system to the detriment of consumers. Clearly defined policies outlining allowable advertisements, if administered prudently, can thwart many of these attacks, but online advertising system are far too large to police manually. Accordingly, modern systems, such as the system monitoring Google's advertisement networks [109], are built on top of large-scale automated and semi-automated machine learning tools designed to aid operators in tackling these problem at scale. Learning algorithms are fast and inexpensive, but are frequently less precise in their classifications, so these systems use machine learning where it consistently works well in catching clear-cut cases, thus allowing technicians to focus on the more difficult borderline cases. Malicious advertisers are constantly devising new strategies to subvert policies. To stay abreast of the rapidly changing landscape of attacks, ground truth data is fed back to the learning system from the human operators as training data and used to retrain the entire system. These systems are, therefore, continually evolving lines of defense designed to most efficiently and effectively leverage human resources to ensure a safe environment for online patrons.

5.1.3 Social media spam

With the recent developments in junk email detection, spam senders changed their targeted communication medium. Nowadays, social networks, social media websites and recommendation services such as Facebook, Google+, MySpace, Twitter, YouTube, Flickr, SoundCloud, TripAdvisor, Amazon, and so forth are the major target for spammers. Most of these services use machine learning methods [75, 116].

Beside distributing "classical" spam, these platforms are also used

- to attract attention by heavily interacting with other users,
- **—** to create fake reviews and thus manipulate recommendations,
- to build fake friend networks to manipulate rankings,
- to start rumors and harass.

 $^{^{3}\} http://www.virusbtn.com/resources/spammers$ compendium

⁴ http://prag.diee.unica.it/pra/eng/research/doccategorisation/spamfiltering/products/imageCerberus

Social media spam differs from traditional email spam in that spammers can exploit many different functions of these websites including posting/reposting comments, sending private or chat messages, following/re-following other users, favoring items, and uploading images/videos/sounds/documents/applications.

Service providers are faced with the problem of distinguishing regular user actions from spammy behavior. This problem appears to be more difficult than detecting classical spam since spammers have many more possibilities to prevent detection. They can hide their activities by mixing them with unobjectionable actions such that the distinction between legitimate and abusive behavior becomes blurred and even humans cannot distinguish them from normal users. As a consequence, ground truth data is very hard to gather and is typically very noisy making this a particularly challenging learning domain.

5.1.4 Plagiarism Detection and Authorship Identification

Plagiarism has been a long-standing plague in academics and media. As shown by the case of two former German ministers, Karl-Theodor zu Guttenberg and Annette Schavan, the discovery of plagiarism may ruin a person's scientific and even political career. The business case for plagiarism is becoming especially important for self-published content, such as Amazon's Kindle Direct Publishing, in which low publication costs and the potential for high distribution volume make it an especially attractive target for providers of non-authentic content. Although most of the previous high-profile plagiarism cases were uncovered by the web-assisted and -coordinated efforts of activists, a significant effort has been put into the development of automatic methods for plagiarism detection. Four plagiarism detection competitions have been held under the aegis of the PAN Conference,⁵ which have attracted significant attention in the machine learning and the information retrieval communities. Several commercial products are available on the market: interestingly, one of the vendors (iParadigms) offers software for both plagiarism detection (Turnitin) and verification of the lack of plagiarism (WriteCheck). Evasion of plagiarism detection system has not been systematically studied, although heuristic obfuscation methods have proved to a significant hurdle for detection accuracy.

A somewhat related problem is authorship identification. Research in this field is motivated by user-generated media, e.g., blogs, which offer ample possibilities for falsification of author identities. The recent case of the fake identity of Amina Arraf in the blog "A Gay Girl in Damascus" has demonstrated that a significant political influence can be exerted by identity manipulation, including the careful adaptation of the forger's writing style. Some recent work (e.g., [1]) has addressed methods for detecting fraudulent writing styles as well as potential evasion techniques.

5.1.5 Copyright Enforcement

Apart from detecting plagiarism and duplicated content in textual documents, social media platforms facilitate the sharing of media files such as images, videos and music, which also must be monitored for copyright infringements. The publication of media content is generally restricted in terms of the usage and the geographical location depending on copyrights and patents. The business model of film studios, music labels, photographers and artists crucially depends on the protection of intellectual property rights.

⁵ http://pan.webis.de/

Social media websites are required by law to effectively identify copyright infringement. Both detection and evasion technologies for copyrighted media content differ radically from the those used for plagiarized text. In the latter case, characteristic features for the learning problems stem from linguistic traits of the content. For media, mostly steganographic methods have been used [55]. These, however, can be easily detected and removed by a technologically proficient offender.

Practical methods for detection of copyright infringement in media are mainly based on content fingerprinting. Even if these methods are computationally efficient, they are not generally robust against adversarial manipulations such as changing the resolution or compression level. Using a larger number of more stable features in combination with statistical learning methods rather than fixed rules can be expected to provide more robust detection.

5.1.6 Computer Vision Systems: Present and Potential Attacks

The application of machine learning to computer vision has a long history because some components of computer vision systems are difficult to manually design, but it is often relatively easy to collect labeled examples from a vision task to train a learning system [86]. This is particularly true for high-level computer vision components devoted to pattern recognition, but learning has also been used in some low- and middle-level vision components [110]. Nowadays many computer vision systems (*e.g.*, face recognition systems and OCR tools) are developed using machine learning or use an online learning module because the resulting systems are more accurate than hand-crafted programs. However, attacks against the learning components of computer vision systems emerged only recently as the application and popularity of these technologies generated sufficient incentives for attackers.

Biometric recognition is an important application of machine learning to computer vision that recently witnessed its first attacks. Indeed, all current biometric recognition systems use machine learning. Face and fingerprints are the most widely used biometric traits and their computerized recognition has been the subject of scientific investigation for many years [82]. These technologies are used now for personal identity verification in passports, personal computers and smart phones. The risk of attacks against biometric recognition systems has been investigated in the scientific literature [14] but the emergence of financial motivations makes it a looming danger. Among the attacks proposed, the most practical is a mimicry attack in which fake biometric traits are used to fool a learning-based recognition module; e.g., using a printed picture to fool a facial recognition system. Such attacks are called *spoofing* attacks, and they have a great practical relevance because they do not require advanced technical skills making them feasible for many potential attackers.⁶ In fact, the winner of the ICB 2013 "spoofing challenge" against face recognition systems was a lady who used a mimicry attack based on facial makeup to claim successfully the identity of a gentleman.⁷ However, spoofing attacks are not limited to face and fingerprint recognition—the European project, TABULA RASA, also demonstrated successful spoofing attacks against systems using speech and gait.⁸

Another little-known type of attack likely to emerge in the near future is an evasion attack against biometric video surveillance systems used to recognize targeted individuals (e.g., individuals on a watch-list). To date this avenue of attack has received little attention

⁶ An example of a spoofing attack: http://www.youtube.com/watch?v=2fKGXSgOFYc.

⁷ http://www.tabularasa-euproject.org/evaluations/tabula-rasa-spoofing-challenge-2013

⁸ http://www.tabularasa-euproject.org

because evading a biometric video surveillance system is still quite easy (wearing hats or glasses is often sufficient to evade a video face recognition system). However, the arms race to evade these vision systems has already begun as is evident in the creative CV Dazzle project that proposes new facial makeup and hair styling to evade face recognition systems.⁹

Incremental learning algorithms are also beginning to be incorporated into adaptive biometric systems to account for natural changes in biometric patterns and the surrounding environment; e.g., the aging of biometric traits or changes in illumination. Indeed all biometric recognition systems require frequent updates of the *templates* used as prototypes for the biometric traits of users, and some systems use self-training algorithms [105]. Recently, it has been shown that an attacker may exploit self-training to compromise the templates of a face recognition system through a poisoning attack [15]. This poisoning attack consists of submitting a carefully designed sequence of fake facial images to the system to gradually perturb the client's template until it is compromised; *i.e.*, when it is replaced with a different face. This may allow an attacker to impersonate the targeted client using her own face.

Finally, another potential class of attacks that may emerge in the near future involves image forensics tools. Nowadays altering digital images with commercial photo-editing tools is commonplace, and this alteration may be used for fraud [42]. As the detection of malicious image alteration can be difficult, digital image forensic tools using machine learning have been designed to detect specific types of alterations (e.g., the deletion of part of image like the face of a person, or a copy-and-paste from one image to another). As in other adversarial applications, we expect an arms race to develop between forgers and forensic analysts, with forgers developing new tricks to evade the current digital image forensic tools based on machine learning.

5.1.7 Sentiment analysis

In recent years, many marketing companies started to apply sentiment analysis (the task of discerning the opinion or partiality of a user from his/her communications and behavior) to become aware of users' preferences on brands, products or services. For example, an online travel agency may want to know the rating of hotels based on the guests' opinions. Instead of performing a potentially time-consuming and costly survey, natural language processing and machine learning can be used to extract this information from public blogs, forums, Twitter feeds, and similar sources.

With the rise of sentiment analysis, pollution attacks will become likely in order to boost one's own image or to defame competitors. Sentiment analysis mainly relies on linguistic or deterministic natural language processing methods which are not robust against data manipulation. Since this kind of analysis is intrinsically unsupervised, poisoning attacks are likely to become a serious issue in the future.

5.2 Recommendations and Research Priorities

Although it is generally hard to define research priorities for the heterogeneous application fields reviewed in Section 5.1, in the following, we attempt to provide some methodical recommendations that may have repercussions in several potential application domains.

⁹ http://cvdazzle.com

5.2.1 Poisoning

Poisoning refers to attacks against machine learning, in which an attacker can insert manipulated data before or during the training phase of a learning system. Poisoning has been identified as a serious threat for specific intrusion detection techniques [96], as well as for general machine learning methods [17, 60, 107]. The importance of protecting against poisoning attacks lies in the fact that many real-life learning systems are periodically re-trained from new data. While re-training helps to keep systems abreast of the natural drift of real data, it can also be abused by attackers if new data is used for training without further control or sanitization. The specific implications of periodic re-training schemes ("quasi-online learning") for poisoning attacks have, to date, only received limited attention [60, 61, 107]. Hence further research is needed to analyze the effectiveness of such attacks and to develop adequate protection mechanisms against them.

5.2.2 Penetration Testing

Penetration testing, for our purposes, is the empirical evaluation of the vulnerabilities of an aggregate system combining multiple applications to malfeasance.¹⁰ This type of security assessment has become a de facto requirement for the majority of web-applications, especially in the financial industry [108]. Many companies are interested in having their systems successfully pass penetration tests. Penetration testing evaluates the company's exposure to security risks and can potentially decreases its premiums for liability insurance. It is conceivable that similar testing requirements will become increasingly adopted in data-driven systems. This would create the need for appropriate penetration testing technologies. Developing these techniques is an interesting research challenge, which crucially depends on the question of whether or not learning systems can be reverse-engineered by a potential adversary.

5.2.3 Case Studies

Being largely an empirical field of science, machine learning typically entails large-scale case studies for the verification of results. It has a long tradition of benchmarking (*e.g.*, the USPS and NIST datasets and the UCI repository of datasets [4, 29]) as well as competitions on various datasets. In contrast, empirical evaluations in the field of computer security, are much more difficult to carry out. The only attempt to comparatively evaluate real intrusion detection systems conducted at MIT Lincoln Lab had limited success and drew a barrage of critical remarks [79, 83]. Several issues that make comprehensive case studies in security related research areas scarce, and which also concern adversarial machine learning, are elucidated below.

5.2.3.1 Privacy issues

Many datasets in computer security and related areas are subject to serious privacy restrictions. To tackle this, an official institute such as NIST may be entrusted with managing such data and with performing standardized experiments. A successful example of such a benchmark was the NIST TREC Spam Track [29], which enabled researchers to compare spam filtering

¹⁰ Penetration testing may also refer to the evaluation of an individual application used in several contexts, but we do not discuss this type of testing here.

techniques in various settings and was based on real world datasets. However, privacypreservation was not an issue for the TREC benchmark because it was constructed using publicly available data particularly from emails obtained from the Enron court case [59]. However, the amount of publicly available data is relatively scarce compared to the amount of data stored confidentially, but maintaining privacy when releasing datasets derived from the latter sources is generally technically difficult, and some examples of privacy incidents related to data release were discussed in Section 4.3.

5.2.3.2 Non-stationarity of the data

As attackers respond to a particular predictive model, static datasets are insufficient; however, dynamic data is difficult to generate under realistic conditions. Test suites can still be defined in terms of rules of "games": *e.g.*, playground.dk where a player takes the role of an attacker of a computer security system. Even if generated data is artificial and differs depending on the method under investigation, the results may be comparable if they are obtained under realistic conditions.

5.2.3.3 Lack of ground truth

In contrast to many other applications of machine learning, ground truth data is hard to obtain in adversarial environments. Defining ground truth for adversarial learning is especially difficult since the concept of abusive behavior is usually quite vague. Furthermore, adversaries attempt to hide their activities so that even humans are not able to identify them. To identify common applications and use cases, it is necessary to formally describe non-adversarial activities for each case, potentially using domain-expert knowledge, and to treat deviations from these allowed activities as adversarial events.

6 Conclusion

Anthony D. Joseph, Pavel Laskov, Blaine Nelson, Fabio Roli, and J. Doug Tygar

As one would expect for a workshop in an emerging discipline, our workshop has raised a broad variety of research questions. Some of these questions stem from fundamental methodological issues, such as the formalization of secure learning and the trade-off between security, privacy, and interpretability of learning models. The workshop has also identified practical open problems; *e.g.*, integrating machine learning with existing security mechanisms and understanding of an operator's role in such a process. Several potential novel applications have also been identified, such as the detection of advanced persisting threats, protection of mobile devices, continuous authentication, and computer forensics. We expect that secure learning will play a crucial and expanding role in a large number of data-driven applications, especially online advertisement, social media and recommendation systems.

Yet the most important outcome of this workshop is the new found sense of an emerging scientific community growing at the junction of computer security and machine learning. It is not easy for researchers in these two fields to communicate with one another. Scientific traditions and practices of machine learning and computer security diverge in many aspects, especially where experimental work is concerned. There indeed exist objective reasons for such divergence. The data arising in computer security is subject to privacy and confidentiality restrictions, which makes the traditional benchmarking practices of machine learning less feasible. On the other hand, the adversarial nature of data is a novel aspect for the machine learning methodology, which requires a thorough recapitulation of its theoretical foundations. To understand these issues, and to bring researchers in these two communities closer to each other, regular scientific exchange is indispensable. Stay tuned for forthcoming events and advancements in this field.

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Manifesto from the Dagstuhl Perspectives Workshop 13342

ICT for Bridging Biology and Medicine

Edited by

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– Abstract

The systems paradigm of modern medicine presents both, an opportunity and a challenge, for current Information and Communication Technology (ICT). The opportunity is to understand the spatio-temporal organisation and dynamics of the human body as an integrated whole, incorporating the biochemical, physiological, and environmental interactions that sustain life. Yet, to accomplish this, one has to meet the challenge of integrating, visualising, interpreting, and utilising an unprecedented amount of *in-silico*, *in-vitro* and *in-vivo* data related to health care in a systematic, transparent, comprehensible, and reproducible fashion. This challenge is substantially compounded by the critical need to align technical solutions with the increasingly social dimension of modern ICT and the wide range of stakeholders in modern health-care systems.

Unquestionably, advancing health-care related ICT has the potential of fundamentally revolutionising care-delivery systems, affecting all our lives both, personally and – in view of the enormous costs of health–care systems in modern societies – also financially.

Accordingly, to ponder the options of ICT for delivering the promise of systems approaches to medical care, medical researchers and physicians, biologists and mathematicians, computer scientists and information–systems experts from three continents and from both, industry and academia, met in Dagstuhl for a Dagstuhl Perspectives Workshop on *ICT Strategies for Bridging Biology and Medicine* from August 18 to 23, 2013, to thoroughly discuss this multidisciplinary topic and to derive and compile a comprehensive list of pertinent recommendations – rather than just to deliver a set package of sanitised powerpoint presentations on medical ICT. The recommendations in this manifesto reflect points of convergence that emerged during the intense discussions and analyses taking place the workshop. They also reflect a particular attention given to the identification of challenges for improving the effectiveness of ICT approaches to Systems Biomedicine.

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32 ICT for Bridging Biology and Medicine

Executive Summary

"Water, water, everywhere, nor any drop to drink."

So goes Coleridge's *Rime of the Ancient Mariner*. Until recently, the same went for data: everywhere, but not of much use so far, neither for deriving new medical insights nor for improving medical care.

However, three key developments currently help to overcome this problem: the rapid adoption of electronic medical records [1], the dramatic advances in molecular biology [2], and, just as dramatic, the growing pervasiveness of social computing environments combined with a new attitude towards participatory health management [3, 4, 5].

The result is an exciting medley of initiatives devoted to supporting health-care related information flow ranging from patient-facing resources such as *PatientsLikeMe* [6] to initiatives such as *MD-Paedigree* [7] (EU's FP7) that provides a physician-centric sort of "*PatientsLikeMine*" analogue addressing treatment choices in paediatrics.

Managing the *creative deconstruction* [8] involved in advancing towards systems medicine requires fundamentally changing the use of ICT in both, health care and biomedical research. It requires in particular to take account of the new paradigm of *web-centric computing* which is a basic prerequisite for all these initiatives.

Reflecting these concerns, a Dagstuhl Perspectives Workshop on *ICT Strategies for Bridging Biology and Medicine* was held to discuss a wide range of fundamental and foundational issues. These ranged from architectural considerations to data-access policies including *Open/Linked Data, the Semantic Web, Pervasive Hardware Ecosystems, Medical Clouds, Patient-Participation Frameworks, "Health Care* 4.0", *Analytical Tools*, and *Medical Education*¹. Clearly, the required changes can only be achieved by initiatives of a broader scale and scope than what can be accommodated within the existing academic organisations, and need to involve all stakeholders at every step of such initiatives. In response to these challenges, the discussions led to the following theses and postulates:

- (i) An *open-data policy* for health-care related information systems is a fundamental and urgent imperative.
- (ii) Following the *business-IT alignment* paradigm [9], health care should on all levels
 be supported by secure IT-platforms enabling clinical workflow engines that map health-care related processes while integrating pertinent data-analysis, visualisation, and engineering tools.
- (iii) Such platforms should also take full advantage of advances provided by *cloud services*, pervasive computing ecosystems, and the semantic web.
- (iv) The *participatory potential* of the Web should be exploited to advance new forms of partnership in the health-care environment.
- (v) The acquisition of *ICT literacy* must become a required part of biomedical education.
- (vi) Specifically in Germany, the Bundesnetzagentur should be encouraged to set up a Working Group Medizinische Netze to explore options for a Medical Cloud within the German health-care environment while for instance in China the new National Health and Family Planning Commission might be the correct organisation to approach.

¹ The raw notes collected during the Dagstuhl Perspectives Workshop can be found at http://bit.ly/dagict.

J.S. Almeida, A. Dress, T. Kühne, and L. Parida

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34 ICT for Bridging Biology and Medicine

1 Introduction

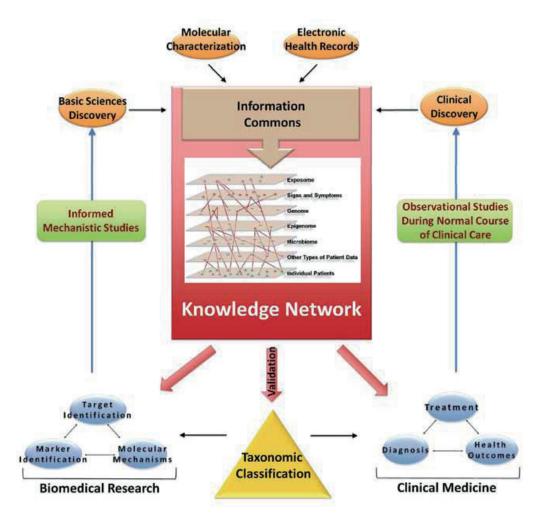
It is a well-known and much deplored fact that, despite of great efforts, much of the overwhelming current progress in bio-medical research does not easily find its way to the bedside. While tools for generating ever better information regarding the individual makeup of a patient are becoming available, the sheer amount of data these tools produce soon becomes overwhelming and cannot easily be interpreted and processed for clinical application by medical practitioners, let alone assist patient engagement within the Health System. And extending medical education further and further has its limits as nobody can encompass and comprehend the onslaught of relevant new medical insights coming along year by year.

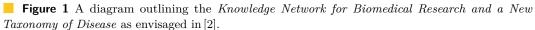
However, there is a growing international consensus that this can be mended using modern process-oriented and integrative ICT-platform solutions including specifically designed *cloud-based and service-oriented architectures*, thus establishing a context-aware computing service infrastructure (as anticipated in [10]) for supporting clinical workflows and connecting bioscience and health care.

The recent report of the National Academies of the USA on *Precision Medicine* [2] provides an excellent starting point for this discussion. It suggests the creation of a framework for a Knowledge Network of Disease (see Figure 1) which could integrate the rapidly expanding range of information on causes and expected progress of diseases. This solution has a number of key advantages over the current insular medical-institution-centric model as it would allow researchers, health-care providers, and the public to share and update their information. It asserts: As well as improving health care, the new data network could also improve biomedical research by enabling scientists to access patient information through electronic health records, while still protecting patient rights. [...] Dramatic advances in research have generated a wealth of new data that could improve health outcomes. However, currently there is a disconnect between scientific advances in research and the incorporation of this information in the clinic. In addition, researchers don't have access to the wealth of clinical data on patients that is collected at the point of care. In order to harness the power of emerging disease data, systems are needed to collect and make the information widely accessible. In a nutshell, a comprehensive ICT solution for Health Care must link and aggregate multiple data sources and provide advanced governance models enabling multiple, potentially disparate, or secondary data usage for operational and research tasks without ever compromising patient rights.

In Europe, the ITFoM initiative [11] states quite dramatically, that currently, a new spectre is haunting Europe and needs to be addressed, the spectre of "aging": Europe ages. Its health budgets soar. Europeans suffer from ill-managed diseases. And all of this against a background of extremely successful life sciences with little societal impact, and revolutionary ICT that seems to affect all areas of society except for medicine. What will Europe do? Wait until the problems disappear? Wait until solutions originate in other countries? Or realise that it is best posed to provide a solution; a revolutionary ICT that revolutionises medicine. And reinforcing ITFoM's expectation of a critical role for ICT in this domain, Google announced soon after the Dagstuhl workshop that it was starting a new company, Calico, with the broad goal of tackling the challenge of aging and associated disease (cf. [12]).

Such insights led to proposing a Dagstuhl Perspectives Workshop on *ICT Strategies for Bridging Biology and Medicine* that then took place in August 2013 and brought together a highly motivated group of leading researchers from academia, research institutions, and industry comprising physicians, medical researchers, biologists, mathematicians, computer scientists, and information–systems experts from 3 continents. Together, they exchanged ideas,





(Reproduced with permission from "Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease", 2011, by the National Academy of Sciences, Courtesy of the National Academies Press, Washington, D.C.)

discussed key challenges, identified urgent tasks as well as long-term strategic opportunities, and explored how integrative ICT architectures can be used in medical care to bridge the widening gap between biomedical research and daily clinical routine. In particular, they discussed the pros and cons of, on the one hand, the more data-driven bottom-up strategy for web-based Big-Data exchange and annotation favoured by the *Semantic Web community* as represented by participants from W3C and from the *Digital Enterprise Research Institute* in Ireland, and on the other hand, by the more model-driven top-down strategy favoured by ITFoM.

In these discussions, it was a point of strong consensus that, as in many other areas that are undergoing a *data science revolution* [13], the development of ICT for the modern health-care environment depends critically on the availability of an *open-data infrastructure* sustaining an information society capable of engineering a knowledge economy [14]. Enabling the Web to form a global and secure space of linked data was therefore seen as a prerequisite for

- managing the creative deconstruction required to fundamentally change the use of ICT and advancing towards systems medicine by creating IT-platforms enabling clinical workflow engines mapping health-care related processes,
- integrating pertinent data-analysis, visualisation, and engineering tools,
- modelling and visualising the spatio-temporal organisation and dynamics of life and disease,
- and unfolding the potential of patient participation employing pervasive hardware ecosystems and medical clouds.

Of course, there are also many ethical, legal, societal, and political issues related to medical ICT that the workshop was not able to cover. Nor did we feel in a position – mainly in view of the strong heterogeneity of the group of participants – to devise a detailed *road map* of further progress going beyond the recommendations reported already above (i.e., our six "theses and postulates").

Instead, the workshop's most crucial insights have been detailed below, beginning with a discussion of critical role of adequate ICT architectures and an open-data policy, and continuing with sections on patient participation, personalised systems medicine, the need of a medical cloud, pervasive systems for medical ICT, process modeling for "Healthcare 4.0", analytical tools, and medical education.

2 The need of adequate ICT architectures

While the emergence of genomics and other *omics* technologies as well as many other data sources (imaging [15], sensoring [16], etc.) have specifically highlighted the critical need for adequate ICT frameworks, ICT plays a decisive role in a much wider range of processes involved in *acquiring*, *managing*, and *processing* all sorts of biomolecular and medical data.

Of course, ICT cannot make clinical decisions. It can only facilitate the access to medical information and support clinical workflow processes. The decisions still have to be made by the physicians (together with their patients) based on their clinical experience as well as information from all relevant sources – including systems-medicine data. ICT should help them to utilise the available data and their clinical experience most productively, to identify suitable experts, and to provide a platform for efficient communication between the concerned parties. That is, adequate ICT architectures must provide medical researchers and practitioners with means to easily and securely

- exchange their views regarding new biomedical developments,
- obtain, annotate, exchange, and interpret their patients' data in the light of the latest biomedical insights taking into account all that can be learned from the various relevant databases and bioinformatics tools the web provides,
- check data consistency and quality (cf. [17], see also [18]),
- specifically search for, collect, and quickly comprehend the most relevant insights exactly when needed and within the context of an efficient clinical workflow,
- derive pertinent predictions regarding their patients' fates on the basis of these data,
- and to discuss the implications of such insights for their clinical work with colleagues, patients, and health managers,
- while simultaneously making change and improvement a daily routine.

Adequate ICT architectures should also be open to involving other stakeholders in the medical environment like patients, nurses, researchers, managers, health-care insurers, or policy makers.

To this end, ICT must establish *network services* supported by associated *workflow engines* and *computing platforms* that enable

- systematic de-coupling of services,
- proper assignment and observance of rights and roles,
- task-dependent dynamic modification of rules, roles, and rights,
- activity monitoring and object management,
- assured security, e.g. by providing cryptographic protocols like *Transport Layer Security* (TLS) or *Secure Sockets Layer* (SSL), and
- mediation of conflicts².

However even today, meeting these demands is not as easy as it may sound. Indeed, the current state of the art is so dire that, for instance, the adoption of Electronic Health Records, spearheaded by the ONC, the Office of the National Coordinator for Health Information Technology [20], has at times been felt to decrease – rather than enhance – the effectiveness of care delivery. E.g., it is deplored for instance in [21] that doctors become increasingly bound to documentation and communication products that are functionally decades behind those they use in their "civilian" life and that most EHR vendors, in order to protect their prices and market share, don't even embrace existing modular architectures with interfaces that allow extension of product capabilities, innovative uses of data, and interoperation with other software.

And young medical professionals confessed in private talks that they are already dreaming of a *de-digitalisation* of medicine as they tend to see ICT in hospitals as a curse, not a blessing for medical care. So, there is an imminent danger that outdated, if not incompetent design of medically oriented ICT will actually be counter-productive, not enhancing the application of information technology in medicine, but stand in its way.

In particular, as *time* is still the most precious resource also in medical care, computer scientists need to find out how to design intelligent ICT so as to simplify the practitioners' professional life, not to overburden it with ever more additional requests, and to save, not to waste their time. Research aiming at improved means of data collection, communication, and

 $^{^2}$ See e.g. [19] for a discussion of divergent innovation priorities among the stakeholders in the medical environment.

visualisation along with more transparent user interfaces for health practitioners, patients, and other stakeholders as detailed for instance in [22] should, therefore, be a key priority.

Cautionary tales also abound in the realm of *biomedical informatics*. For example, the ICT associated with *The Cancer Genome Atlas* and the *International Cancer Genome Consortium* has, in spite of the tremendous value delivered by the data it contains, not proven to be as helpful as was expected. And, much more worrisome, the *Cancer Biomedical Informatics Grid* initiative was explicitly found to having directed hundreds of thousands of dollars to ICT developments that, in fact, did more harm than good [23, 24].

3 An open-data policy for the health-care community

As mentioned above, while ICT is being quickly commoditised and Big Data already pervade all ICT arenas of economic, medical, and research activities [25, 26], creating

- flexible open-data structures,
- linked open-data (LOD) web-technologies (as demanded e.g. by Sir Tim Berners-Lee in his celebrated call for *Raw Data Now* [27, 28, 29]),
- and transparent data-analysis tools delivering comprehensible, reproducible, and reliable results [22, 30, 31, 32]

is becoming a top priority in the context of medical ICT.

It is important to clarify that the call for an open-data policy is a call for open standards and interoperable systems. It is by no means a call that private data be forcefully made public. Yet, not adopting an open-data policy for public data was seen in this workshop as nothing short of unacceptable. More specifically, as emphasised for instance by William Hersh in his slide file *Translational Research: The Essential Role of Biomedical Informatics* [33], the required open-data policy for health-care related information systems includes:

- an open development of tools and infrastructure created by an open, participatory process,
- open access to resources that should be freely obtainable for the health-care community,
- and an open source code that is available to view, alter, and redistribute.

Health care is now seriously lagging behind other data-intensive activities in its ability to realise the benefits of data integration and secondary use of publicly funded data resources. In conclusion, at a time when the web is evolving to become a global data space, the request of an open-data policy in health-care related information systems was therefore one of the most urgent and most consensual demands expressed by the workshop participants. More specifically, adopting the World Wide Web Consortium's *Resource Description Framework* (RDF) [35, 36] was seen as a particularly helpful strategy to achieve the goals of this policy.

Similar consensus was found with regard to

- the adoption of public-data dissemination policies with moratoria not longer than 6 months
- and the request that any future publicly funded large-scale research project should be required to only use – or re-use – infrastructures that are scalable and can manage Big Data.

4 Patient participation

Clinical and molecular stratification of disease in patient populations [37], combined with the commoditisation of ICT, has empowered patients in unprecedented ways. The disruptive nature of this process, epitomised by initiatives such as PatientsLikeMe [6] or Leroy Hood's P4-medicine initiative [38, 39], is further deepening the integration of ICT into health-care activities and the health sciences. The control of this process is increasingly distributed and requires a new partnership in the health-care environment in order to advance and exploit – rather than to (hopelessly) curtail – the participatory nature of the system.

Such developments need to be pursued more aggressively if the health sciences – and health care in general – are to catch up with the fast-paced societal changes associated with the emergence of third-generation web and social computing technologies. And as ICT is increasingly provided to patients via new platforms such a mobile apps, this is in fact a development which, while inevitable, is clearly offering a promising route to make patient participation a key feature in improving outcomes and decreasing costs – a fact that is just starting to be recognised in academic and medical institutions.

However, adequate participatory systems do not yet exist, and just installing an open-data policy – though crucial as it is – will not be enough to bring such systems into existence. To encourage and support participation and cooperation, any open-data policy has to be augmented by an overall redesign of current health information systems constructing and maintaining systems that properly assign rights and roles, thus making participation and collaboration simple and secure while respecting the sharing preferences of the involved patients.

Yet, unlike the Open Data recommendation where even the technical details were clear, the best route towards patient participation is uncertain. For example, ownership of one's own data is seldom supported by current ICT in health-care related information systems.

Therefore, a new way has to be found. In consequence, a number of (not at all mutually exclusive) options were discussed by the participants:

- integrating all local and more or less isolated health-care related information systems within a shared, secure, and well-maintained cloud environment,
- developing software for merging data of different structure and from different sources while still guaranteeing data quality [17, 18], security [34], and privacy [40],
- and deploying systems that assign rules, roles, and rights in a dynamic way allowing for continuous modifications (see e.g. [41]) and for managing and resolving emerging conflicts as an integral part of the system.

The pursuit of each of these routes is fraught with practical difficulties. For example, managing change and dynamic modifications of rules, roles, and rights in the ICT landscape implies obtaining and maintaining patient consent for data sharing. However, obtaining informed consent is itself often a primitive process that often discourages the use of ICT tools – even by patients who overwhelming express a desire to share their data. Assuring the privacy and security of data, once shared, is even more complex as patients express great concern about subsequent misuse [34]. Patient access to health data is also impeded by complex and often inconsistent terminologies, and further complicated by the lack of effective mechanisms to validate agreed governance policies.

The lack of specific recommendation beyond the encouragement of patient participation is in stark contrast with the growing adoption of document-sharing platforms such as DropBox and Google Drive, or even Facebook. These user-facing tools have a mass appeal and find

an increasing use in health-care environments – often in contravention of explicit policies disadvising them sternly. Judging from the strong movement towards *client-facing ICT* in other data-intensive domains such as banking, transportation, and retail, the most effective recommendation here may well be that already the design of participatory medical ICT needs the participation of patients and patient organisations.

Nevertheless, there may be instances where the pursuit of patient participation leads to results that are the opposite of those intended. For example, special attention has to be given to the elderly as well as to the computer illiterates to avoid their discrimination and adding to health disparities that already exist.

5 Creative deconstruction

Managing the *creative deconstruction* [8] involved in advancing towards personalised systems medicine requires a fundamental change in the use of ICT in both, health care and biomedical research and modelling.

We are all different. Diseases are different. We react differently to the same therapy even if we have the "same" disease. Only an ICT-driven big-data medicine that takes advantage of the vast amount of personalised and research data available can help to take this individuality into account, providing better therapies at ultimately lower cost.

Indeed, the costs of sequencing a person's genome have dropped by close to a million fold in a bit more than a decade. Moreover, the needed information and communication technology is rapidly becoming inexpensive enough for routine clinical use. A modern tablet computer, while costing only a few hundreds of dollars, now has the power of a high-end computer of only a few years ago. And their power continues to grow by roughly three orders of magnitude every decade.

In consequence, we have a chance to change the lives of many by redesigning the mechanisms in health-care delivery to take full advantage of the enormous power of new computational resources and analytic tools as detailed below.

However, despite this exciting promise, many processes in medicine have hardly changed over long periods of time. If we bring our car to the garage for a service, the mechanic will be able to analyse megabytes of information, allowing a much more 'personalised' correction of problems than we are likely to receive from our doctors to whom typically only a minute fraction of the information is available compared to the information the mechanics have on our car. It is time

- to think ahead which effect these continuing changes of many orders of magnitude could have on health-care systems,
- to address their enormous potential for health care and biomedical research and modelling,
- to consider radical changes as we face radical challenges in ageing societies, and
- to plan ahead for the future rather than to continue reacting after the fact with incremental adjustments – always too little too late – to these predictable developments once they have happened. Our lives as well as even the financial and social stability of our societies might be at stake.

The workshop participants also agreed that the required changes can only be achieved by initiatives of a broader scale and scope than what can be accommodated within existing academic organisations while the fact that most health care is delivered in community

practices, not in academic institutions, was seen as a decisive motivation for always involving medical practitioners and other stakeholders in the medical environment at every step in all such initiatives.

Depending on local conditions, this could be pursued by initiating pertinent calls for tenders, setting up appropriate working groups, or establishing suitable new institutes, cross-institute initiatives, or national or international branches of ICT or health-care related organisations.

Such organisations do exist already in the US: the Office of the National Coordinator for Health Information Technology (ONC) is already mandated to support the adoption of health information technology and the promotion of nationwide health information exchange to improve health care [20] (though currently challenged to take the next step: fitting EHRs into a dynamic, state-of-the-art, rapidly evolving information infrastructure rather than jamming all health care processes and workflows into constrained EHR operating environments [21]). And the National Institutes of Health's autonomous *Big Data to Knowledge* (BD2K) initiative [26] might also be a good model to follow.

In Germany, a first step could be to contact the *Gesundheitsforschungsrat* proposing to set up a "Arbeitsgruppe Medizin" within the framework of its *Bundesnetzagentur*, involving also the newly founded *German Centers of Health Science* (Deutsche Zentren der Gesundheitsforschung DZG, cf. [42]).

And in China, authorities on many different levels could get involved with such activities, from the federal level like e.g. the new *National Health and Family Planning Commission* to provincial and prefectural level down to the level of counties and townships.

Such initiatives could also offer a fast route to incorporating the advances of modern medicine in daily health care in third-world countries.

6 The need of a medical cloud

Remarkably, the new paradigm of *cloud-computing* seems to be able to address many of the requests regarding e.g. the performance of adequate ICT architectures, the introduction of open data policies, and the support of patient participation. A broadband-supported interoperable public cloud infrastructure distributed between a multitude of nodes connected by an appropriately designed enterprise service bus [47], could offer "abstract" services (on request and according to well-defined protocols)

- to rapidly and securely store, access, annotate, process, interpret, exchange, and discuss immense amounts of data stretching from family-health histories to health-event logs, medical image data, and genomic information,
- to inspect medical and life-science databases,
- to enable effortless, yet well-protected data management and data communication to support e.g. joint expert online-discussions regarding specific medical implications in the light of newest medical insights,
- to introduce transparent governance models that do not rely on "security by obscurity" and do not compromise interoperability or involve unscalable formalisms,
- and, thus, to escape the current EHR trap deplored in [21] and to regain control of the configuration of EHR infrastructures that most medical professionals are currently only allowed to manage,

The reliance on cloud services for biomedical *research* is now a tried and tested possibility, as illustrated by the research-driven Europe-wide Elixir network [43].

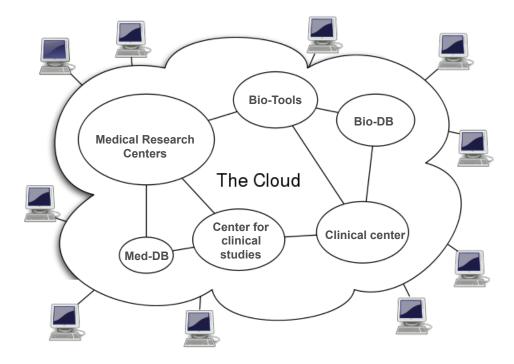


Figure 2 A cartoon of a medical cloud connecting stakeholders in the health-care environment, medical and bio-data bases, and analytical tools (as described e.g. in [44, 45, 46]).

There are legitimate concerns about assuring privacy, security and trust in health data stored in the cloud. They can and must be addressed and they should be object of continued research and advancement.

Nevertheless, the time to initiate the development of cloud services in support of *health-care delivery* is now.

7 Pervasive systems for medical ICT

Pervasive computational systems are among the most recent, promising, and disruptive developments in medical ICT. They range from the usage of standard laptop computers, tablets, terminals, and phones to more specific home-based web appliances (such as wireless weight-scale and blood-pressure measuring devices) and webApp ecosystems (browser hosted software applications – a topic of the next *Conference on Semantics in Healthcare and Life Sciences* CSHALS 2014). There is a mounting profusion of web-connected sensing devices in varying stages of development. Some are ubiquitous in their distribution, some are wearable mobile devices, and still others are intended for use only in the home.

This is an area where research towards a systematic approach to their deployment and integration is only taking its first steps. Early results suggest that this is one of the most important innovations for the future health care systems. It will have an impact that spans from novel opportunities to deliver care at the patients' home, to laboratory medicine that is not only integrated, but in fact involved in the choice of therapy. The transformative nature of these opportunities suggests that the work towards the development of pervasive ICT for health care systems needs to be specifically targeted by research programs.

In a recent survey regarding the *Grand challenges in interfacing engineering with life sciences* and medicine [48], pervasiveness and pre-emptiveness were described as the missing "P's" in the engineering of P4 Medicine. Accordingly, also the development of *Biomedical Systems Engineering Programs* was proposed to be of critical strategic value.

8 Process modeling for "Healthcare 4.0"

The intensive monitorisation, formal description, and exhaustive representation of clinical workflows and other medical processes are the collective blind spot of present-day health sciences. This is not so much a problem that is specific to medicine as it is a reflection of an early stage in the development of industrial processes capable of coping with complex systems. In Germany, the development of high-tech "smart processes" was dubbed *Industrie* 4.0 [49] and described as a new (the fourth!) industrial revolution. Here, a plethora of manufacturing processes reacts to specifications characterised by strong customisation of products under the conditions of highly flexibilised (mass-)production. The required automation technology is improved by the introduction of methods of self-optimisation, self-configuration, self-diagnosis, cognition, and intelligent support of workers in their increasingly complex tasks.

This is also seen as an apt description of what is desirable for the future of ICT in the medical environment. Following the business-IT alignment paradigm [9] mentioned already, health care should – on all levels – be supported by secure IT-platforms enabling clinical workflow engines that map health-care related processes while integrating pertinent data-analysis, visualisation, and engineering tool. The key advantage of this novel approach to process specification is that it promises to remove the intrusive nature of current health-related ICT that often disrupts, rather than assists, the development of integrated and efficient care-delivery practices.

However, given the early stage of development of this new system, it still needs to be explicitly demonstrated, e.g. by comparative effectiveness research, that the envisaged new clinical-workflow platforms can be used easily and deliver improved clinical outcome and cost effectiveness.

9 Analytical tools

The key role played by data processing, modelling, visualisation, and disease- and patientstratification tools in systems medicine is at the core of the personalisation of health-care delivery. The data-analysis pipeline is also where advances in medicine find their way to preventive medicine. Advances in mechanistic modelling exploiting the spatio-temporal organisation and the dynamic nature of life and disease for generating virtual-patient models (see e.g. [11]), in data mining (see e.g. [44, 45]), and in machine learning, as illustrated by its iconic use of IBM's Watson [46], are among the most promising developments in biomedicine. On the other hand, this remains an area hampered by serious availability and reproducibility issues [30, 31, 32]. Interestingly, these are issues that reflect the lack of integration of present-day computational statistics environments rather than an inherent limitation of discriminant-analysis techniques (including machine learning). In other words, the main

barrier to a wider availability of advanced analytical tools is to be found in the ICT infrastructure, not the analytical methods per se.

Accordingly, the recommendation regarding analytical tools is that the data-processing environments be selected on the basis of their ability to take full advantage of advances towards open data (Section 3), pervasive systems (Section 7), and cloud services (Section 6).

10 Medical education

The last half-day session of the Perspectives Workshop was entirely dedicated to education and workforce issues. The ongoing advances in medicine, particularly the increasing sophistication of ICT and the growing role of patient participation, necessitate that the acquisition of appropriate ICT literacy must be supported in biomedical education, and incorporated as a required part into the teaching of medicine, nursing, and other health professions.

While no specific route has been suggested, it was noted that, in the US, Clinical Informatics is emerging as a board-certified medical subspecialty within Pathology [50]. Public Health and Genetics were also considered.

Also, an argument was made that ICT topics are best introduced at an early stage of medical training, particularly since they are already being added to primary and secondary education [51]. Medical education and workforce training in health-related ICT will have to be a core mandate of any initiative claiming leadership in this field. Ultimately, the goal is to equip and empower physicians, nurses, and other care providers to assist patients with the assimilation of what will otherwise be an overflow of information about themselves. Given the time it takes to realise investments in education and workforce training, the integration of ICT topics in medical programs is an *urgent* matter.

The acquisition of ICT literacy – including an education in the utilisation of "high-dimensional" data – is an important point not only in medical and biomedical education, but also for the public in general (comprising, of course, also *future* patients and medical practitioners, nurses, policy makers, etc.) and requires a more quantitative approach to the teaching of Science and Technology at the K-12 education.

11 Overview of the Program

During the workshop, the following topics were addressed in regular sessions, complemented with impromptu evening presentations and discussions. Rapports for each of them were produced and later collected at http://bit.ly/dagict:

- 1. Information and Communication Technology for Bridging Biology and Precision Medicine – Chances and Challenges
 - From web appliances to web services
 - From home medicine to cloud-based health information systems
 - From laboratory systems to reference genomic atlases
 - Architectures and APIs for user-governed ICT

Coordinator: Jonas S. Almeida

Contributors: Hans Lehrach, Wolfgang Maass, ...

Rapporteur: Mark Braunstein

2. Big and Heterogenous Data

- What can Big Data tell us?
- Genomic Medicine
- The integration and modeling of heterogenous multi-omic and imaging data from disease and its implications for diagnosis and therapy
- Fusing bioimaging data with clinical and molecular information (for enhancing a systems view of disease)

Coordinator: Joel Saltz

Contributors: Klaus Maisinger, Stefan Decker, Scott Kahn, ...

Rapporteur: Alex Pothen

3. How can ICT help us learning more about disease mechanisms?

- Architectures and APIs for user-governed ICT
- Medical Clouds as platforms for annotation, exchange, and joint interpretation of healthcare data by medical experts (and patients?)
- Statistics, machine learning etc.
- Electronic health records
- Coordinator: Bernhard Balkenhol

Contributors: Eric Neumann, Eric Gordon Prud'hommeaux, \ldots

Rapporteur: David Gilbert

4. Virtualisation, Computation, and AI in Medicine

- The status of structured (pathway, model etc) databases
- The virtual oncology, diabetes, ... patient in medical practice
- Mechanistic models
- The vision of ITFoM
- How can we extract information from the scientific literature as well as from 'low-grade information' in the web (text mining, the semantic web in healthcare, search strategies in semantic webs)?
- Virtualisation in drug development

Coordinator: Hans Lehrach Contributors: Laxmi Parida, Pietro Lio', Joel Saltz, ... Rapporteur: Andrea Splendiani

5. Molecular Systems Medicine and ICT I

- Assessing emergent properties of chronic diseases and disease mechanisms:
 - The dynamics of disease progression, implications for disease mechanisms
 - Parallel toponome decoding and genome sequencing
 - Cancer and the immune system
- Family genome and tumor genome sequencing the use of Next Generation Sequencing and its implications for therapy and disease stratification

Coordinator: Peter Walden Contributors: Walter Schubert, Robert Burk, Markus Löffler, ... Rapporteur: Eric Gordon Prud'hommeaux

6. Molecular Systems Medicine and ICT II

A systems approach to diagnostics (including the use of proteins, mRNAs and miRNAs from blood and from tissue)

- Biomedical engineering and systems-optimisation strategies in medical care
- Assays for wellness
- Precision medicine and guidelines for evidence-based medicine: complementary or incompatible?

Coordinator: Ina Koch Contributors: Anja Hennemuth, Helena F. Deus, Susana Vinga, ... Rapporteur: Laxmi Parida

 The Stratification of Disease into Discrete Subtypes and its Implications for Science, 'Medical Ontology', Diagnosis, and Therapy Coordinator: Markus Löffler

Contributors: Mark Braunstein, Eric Prud'hommeaux, Peter Walden, ... Rapporteur: Susana Vinga

8. Does the Potential of ICT in Medical Care Require New Forms and Levels of Medical Training, Medical Data Collection, Storage, and Reproducibility, Clinical Logistics, Clinical Trials, and Patient Participation?

Coordinator: Susana Vinga Contributors: David Gilbert, Jochen Dreß, ... Rapporteur: Ina Koch



Figure 3 The *word cloud* for the combined reports of all regular sessions and evening presentations, reflecting the central focus on open data, nucleating discussions about medical information systems, and disease modeling.

12 Final Remarks

We suggest that our recommendations be discussed, modified, and further improved by the Dagstuhl Scientific Directorate and appropriate committees of the GI to be then submitted to the pertinent authorities in governments and professional societies.

We propose in particular that research funding organizations are specifically encouraged to initiate specially funded programs for supporting technology and research projects pursuing these goals.

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