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Chapter 1 : Software Testing

Testing a web application is not easy than testing a static website but not much difficult than testing an e-commerce website. Functionality testing is the most important thing to be performed while testing a web application.

Visual Design 7 Summary: To ensure that people understand the meaning and purpose of icons, conduct multiple types of tests at various stages of the product-development cycle. Designers often rely on icons to save space and to take advantage of the speedy recognition of visuals. With increasing popularity of small-display devices â€" smartphones, wearables, and so on â€" the use of icons has likewise increased. But, how usable are these icons? The only way to know whether a particular icon will work is to test it with users. Different testing methods address different aspects of icon usability. But what makes an icon usable? Here are 4 quality criteria for icons: Can people find the icon on the page? Do people understand what the icon represents? Can users correctly guess what will happen once they interact with the icon? Is the icon aesthetically pleasing? All of these issues will be critical for the success of the final design, but must be considered separately to determine how to improve an icon. Methods for Icon Testing There are several techniques for evaluating icon designs, and which one you use will depend on your goals and on your stage of design. The methods can be separated into 2 main categories: More importantly, however, is choosing a method based on what you need to learn in order to move forward with your design confidently. Keep in mind that, even with methods where the icon is presented out of context, your test participants should always be part of the intended target audience and thus familiar with the overall industry and with relevant concepts. Findability Methods To gauge findability, icons must be shown in their native habitat â€" in the context of the full interface. In-context testing can help you determine if multiple icons appear too similar and users will have a difficult time distinguishing among them, or if the icon is hidden under a false floor or in an ad-rich area and is thus overlooked. Time-to-locate tests are the best measurement of whether or not users can easily find an icon or some other interface element among the crowd of the full design. In these tests, participants must click or tap the UI element to achieve a given task. Measure how long it takes people to successfully select the correct icon, as well as the rate of first-click selections that is, how often their first click is on the right icon: Recognition Methods Testing for recognition is best done out-of-context: Users presented with an icon must guess what that icon symbolizes. In some ways, this is the icon version of a Rorschach inkblot test. The purpose of this test is to make sure that icons are recognizable, and that people can easily deduce the object that it depicts. If you know that your icon will be accompanied by text, you may think that it would be reasonable to show users the label and ask them to select the icon that best represents that label among several possible options. This testing method therefore only makes sense in cases where users would somehow already know to look for a particular functionality within an interface, and are simply trying to locate a matching graphical representation which is not a common circumstance. Information-Scent Methods What matters in the end is not only whether users can recognize what real object the icon resembles , but also if they can infer what functionality that icon may stand for. The same out-of-context testing method used to assess recognition can also be applied to judge information scent. However, rather than simply asking people what the icon may represent, instead ask what they would expect to happen if they selected that icon. Unlike for recognition tests, you should provide some minimal contextual information about the type of system where that icon will appear. For instance, study participants may be told that a suitcase icon is part of an e-commerce website and asked to guess what the icon may denote in the context of that type of website. Note however that no specific information about what that website may look like, nor any hints to possible functionality are actually provided to the users. Measure any difference in interaction rates between versions of the icon, as well as whether users click on the icon and go back to the original page very quickly. This behavior is called probing, and usually is a signal of poor information scent; it indicates that users were disappointed in the content behind the icon and hence returned to the prior page. Be sure to maintain the same position and label for the icons when testing for the optimal graphic, to make sure that no other variable produced the change in user behavior. Attractiveness Methods Besides testing for recognition, icons should also be tested for

attractiveness, both individually and as part of an icon family. One of the common reasons to use icons in the first place is to add visual appeal to a design, but not all icons are equally good-looking. The simplest attractiveness test is to ask people to score each icon on a 1â€”7 scale. If you have alternative designs of the same icon, you can also ask people to pick the most attractive from each set of alternatives and explain why they like or dislike particular images. Finally, you can show people an entire icon family and ask them to pick out the one they like the best and the least. This last test can help you avoid the common problem where most of your icons are fine, but there are one or two less attractive ones that require a do-over to better match the aesthetic of the full design. Standard Usability Testing and Icon Testing Standard usability testing can also reveal issues with an icon. However, keep in mind that there can be many reasons why an icon may be ignored in a standard usability test, some unrelated to the usability of the icon per se. For example, users may get distracted by some other elements in the interaction or in the site design and may not get to ever complete the task. Because of the multitude of factors involved, you should not rely on standard usability testing as the only way to determine the usability of your icons. Phases of Product Development Like with all UX research methods , when choosing a testing method for your icons consider the current stage within the project lifecycle. In this early concept phase, focus on methods to ideate and explore numerous design options. Out-of-context techniques for recognition and information scent are the most applicable during this time, to determine the feasibility of using icons at all and to hone in on the appropriate mental models for the icons. During this designâ€”andâ€”implementation stage, focus on research methods that will continually guide you toward the best icon design for your system. Once icon designs are recognizable, focus on out-of-context testing for attractiveness until clear winners emerge. Once more of the UI is designed, transition to in-context icon-testing methods. Time-to-locate testing is helpful to quantify the findability of an icon and its placement within several potential variations of the interface. Usability testing beginning with paper prototypes and transitioning to higher fidelity versions can give you some additional insights about the expected meaning for icons and their discoverability. Once the system or feature is launched, methods that measure success and allow for incremental improvements are the most applicable. Benchmark testing with usability studies and time-to-locate tests can be conducted periodically to track performance. Other Considerations As with all methods of research, be sure to avoid introducing biases in tests. Pay particular attention to the terms used in the phrasing of tasks, as they can easily prime the imagery associated with the icons. Especially for out-of-context testing methods, consider conducting the study multiple times with various ways to phrase the survey question using synonyms, omitting branded terms, and so on to ensure that task wording did not influence the response selection. Not all these testing methods need to be used in order to reach a usable icon design, but they are each helpful for different purposes and at different stages of the design process. Additionally, each method should be used iteratively, to incrementally move toward a meaningful iconâ€”label relationship, and an optimal placement within the interface.

Chapter 2 : Principles and Applications of Operations Research

Next generation sequencing is a method of DNA sequencing to determine the appropriate order of nucleotides within a DNA molecule. Next generation sequencing technology enables speedy sequencing and produces million of DNA and RNA series with using next technology sequencer.

The importance of any particular factor varies from application to application. In the typical business system usability and maintainability are the key factors, while for a one-time scientific program neither may be significant. Our testing, to be fully effective, must be geared to measuring each relevant factor and thus forcing quality to become tangible and visible. The drawbacks are that it can only validate that the software works for the specified test cases. A finite number of tests can not validate that the software works for all situations. On the contrary, only one failed test is sufficient enough to show that the software does not work. Dirty tests, or negative tests, refers to the tests aiming at breaking the software, or showing that it does not work. A piece of software must have sufficient exception handling capabilities to survive a significant level of dirty tests. A testable design is a design that can be easily validated, falsified and maintained. Because testing is a rigorous effort and requires significant time and cost, design for testability is also an important design rule for software development. For reliability estimation [Kaner93] [Lyu95] Software reliability has important relations with many aspects of software, including the structure, and the amount of testing it has been subjected to. Based on an operational profile an estimate of the relative frequency of use of various inputs to the program [Lyu95] , testing can serve as a statistical sampling method to gain failure data for reliability estimation. Software testing is not mature. It still remains an art, because we still cannot make it a science. We are still using the same testing techniques invented years ago, some of which are crafted methods or heuristics rather than good engineering methods. Software testing can be costly, but not testing software is even more expensive, especially in places that human lives are at stake. Solving the software-testing problem is no easier than solving the Turing halting problem. We can never be sure that a piece of software is correct. We can never be sure that the specifications are correct. No verification system can verify every correct program. We can never be certain that a verification system is correct either. Key Concepts Taxonomy There is a plethora of testing methods and testing techniques, serving multiple purposes in different life cycle phases. Classified by purpose, software testing can be divided into: Classified by life-cycle phase, software testing can be classified into the following categories: By scope, software testing can be categorized as follows: Correctness testing Correctness is the minimum requirement of software, the essential purpose of testing. Correctness testing will need some type of oracle, to tell the right behavior from the wrong one. The tester may or may not know the inside details of the software module under test, e. Therefore, either a white-box point of view or black-box point of view can be taken in testing software. We must note that the black-box and white-box ideas are not limited in correctness testing only. Black-box testing The black-box approach is a testing method in which test data are derived from the specified functional requirements without regard to the final program structure. Because only the functionality of the software module is of concern, black-box testing also mainly refers to functional testing -- a testing method emphasized on executing the functions and examination of their input and output data. In testing, various inputs are exercised and the outputs are compared against specification to validate the correctness. All test cases are derived from the specification. No implementation details of the code are considered. It is obvious that the more we have covered in the input space, the more problems we will find and therefore we will be more confident about the quality of the software. Ideally we would be tempted to exhaustively test the input space. But as stated above, exhaustively testing the combinations of valid inputs will be impossible for most of the programs, let alone considering invalid inputs, timing, sequence, and resource variables. Combinatorial explosion is the major roadblock in functional testing. To make things worse, we can never be sure whether the specification is either correct or complete. Due to limitations of the language used in the specifications usually natural language , ambiguity is often inevitable. Even if we use some type of formal or restricted language, we may still fail to write down all the possible cases in the specification. Sometimes, the specification itself becomes an intractable problem: And people can seldom

specify clearly what they want -- they usually can tell whether a prototype is, or is not, what they want after they have been finished. Specification problems contributes approximately 30 percent of all bugs in software. It is not possible to exhaust the input space, but it is possible to exhaustively test a subset of the input space. Partitioning is one of the common techniques. If we have partitioned the input space and assume all the input values in a partition is equivalent, then we only need to test one representative value in each partition to sufficiently cover the whole input space. Domain testing [Beizer95] partitions the input domain into regions, and consider the input values in each domain an equivalent class. Domains can be exhaustively tested and covered by selecting a representative value s in each domain. Boundary values are of special interest. Experience shows that test cases that explore boundary conditions have a higher payoff than test cases that do not. Boundary value analysis [Myers79] requires one or more boundary values selected as representative test cases. The difficulties with domain testing are that incorrect domain definitions in the specification can not be efficiently discovered. Good partitioning requires knowledge of the software structure. A good testing plan will not only contain black-box testing, but also white-box approaches, and combinations of the two. White-box testing Contrary to black-box testing, software is viewed as a white-box, or glass-box in white-box testing, as the structure and flow of the software under test are visible to the tester. Testing plans are made according to the details of the software implementation, such as programming language, logic, and styles. Test cases are derived from the program structure. White-box testing is also called glass-box testing, logic-driven testing [Myers79] or design-based testing [Hetzel88]. There are many techniques available in white-box testing, because the problem of intractability is eased by specific knowledge and attention on the structure of the software under test. The intention of exhausting some aspect of the software is still strong in white-box testing, and some degree of exhaustion can be achieved, such as executing each line of code at least once statement coverage , traverse every branch statements branch coverage , or cover all the possible combinations of true and false condition predicates Multiple condition coverage. Test cases are carefully selected based on the criterion that all the nodes or paths are covered or traversed at least once. By doing so we may discover unnecessary "dead" code -- code that is of no use, or never get executed at all, which can not be discovered by functional testing. In mutation testing, the original program code is perturbed and many mutated programs are created, each contains one fault. Each faulty version of the program is called a mutant. Test data are selected based on the effectiveness of failing the mutants. The more mutants a test case can kill, the better the test case is considered. The problem with mutation testing is that it is too computationally expensive to use. The boundary between black-box approach and white-box approach is not clear-cut. Many testing strategies mentioned above, may not be safely classified into black-box testing or white-box testing. It is also true for transaction-flow testing, syntax testing, finite-state testing, and many other testing strategies not discussed in this text. One reason is that all the above techniques will need some knowledge of the specification of the software under test. Another reason is that the idea of specification itself is broad -- it may contain any requirement including the structure, programming language, and programming style as part of the specification content. We may be reluctant to consider random testing as a testing technique. The test case selection is simple and straightforward: Study in [Duran84] indicates that random testing is more cost effective for many programs. Some very subtle errors can be discovered with low cost. And it is also not inferior in coverage than other carefully designed testing techniques. One can also obtain reliability estimate using random testing results based on operational profiles. Effectively combining random testing with other testing techniques may yield more powerful and cost-effective testing strategies. Performance testing Not all software systems have specifications on performance explicitly. But every system will have implicit performance requirements. The software should not take infinite time or infinite resource to execute. Performance has always been a great concern and a driving force of computer evolution. Performance evaluation of a software system usually includes: Typical resources that need to be considered include network bandwidth requirements, CPU cycles, disk space, disk access operations, and memory usage [Smith90]. The goal of performance testing can be performance bottleneck identification, performance comparison and evaluation, etc. The typical method of doing performance testing is using a benchmark -- a program, workload or trace designed to be representative of the typical system usage. It is related to many aspects of software,

including the testing process. Directly estimating software reliability by quantifying its related factors can be difficult. Testing is an effective sampling method to measure software reliability. Guided by the operational profile, software testing usually black-box testing can be used to obtain failure data, and an estimation model can be further used to analyze the data to estimate the present reliability and predict future reliability. Therefore, based on the estimation, the developers can decide whether to release the software, and the users can decide whether to adopt and use the software. Risk of using software can also be assessed based on reliability information. There is agreement on the intuitive meaning of dependable software: The robustness of a software component is the degree to which it can function correctly in the presence of exceptional inputs or stressful environmental conditions. It only watches for robustness problems such as machine crashes, process hangs or abnormal termination. The oracle is relatively simple, therefore robustness testing can be made more portable and scalable than correctness testing.

Chapter 3 : Whole genome sequencing - Wikipedia

Today, whole genome sequencing is mainly used in research, but there are several companies that can sequence your DNA. These are known as direct-to-consumer tests. The testing that is offered through a physician is currently several thousand dollars.

For more information on the paper and pencil application procedure click here. The available test dates and times are displayed in real time. Allow days for application processing. Once application is approved, schedule exam at a PSI testing center. Exam sessions are available at least 6 weeks in advance. You will have the best opportunity to schedule your preferred date if you contact PSI weeks prior to your preferred date. Your complete application should be received 6 weeks in advance of the date you wish to take the exam. SOCRA is not responsible for lost or misdirected applications. SOCRA will NOT be able to consider candidates who are unable to provide the requested supporting documentation regarding their experience in clinical research. The submitted application should be fully and legibly completed. Incomplete or illegible applications will not be accepted. Applications and corroborating documentation must be completed in the English language. Payment must accompany your application packet in order to be reviewed. There is an additional fee for the computer based testing option. If payment is by personal or company check, the application packet and check must be mailed together. If you have a disability or special need that prohibits you from taking the examination under standard conditions, please contact the SOCRA administrative office prior to submitting your application to confirm what documentation must accompany your application. Application Review Applications will be reviewed within 5 business days of receipt. Applicants may be contacted by email or phone if additional information is needed to complete their application. Enrollment is NOT confirmed until the application is complete and has been approved. Application Determination Applicants will be notified via email to advise if their application is accepted or denied. Once the application is approved, fees are non-refundable. To schedule an exam date , candidates contact PSI via phone or web registration and select a specific date, location and time. PSI provides candidates with a test confirmation email including date, location, time and directions to PSI test center. If candidate fails to show at designated time and location for exam, candidate will forfeit the CBT fee The applicant MUST bring photo ID in order to be admitted to the examination site.

Chapter 4 : Clinomics Program - Mayo Clinic Center for Individualized Medicine

The report on the Global Mobile Application Testing Solution Market is a meticulous piece of work and is collated by conducting both primary as well as secondary research.

Getting covered Did You Know? Whole genome sequencing is different than gene sequencing. Researchers like this method because it is faster and cheaper. Many questions remain for researchers, health professionals, and policymakers. They can tell you that you are at a higher risk of disease, but the personal choices you make and the environment in which you live still play a very important role. It is important to maintain a healthy lifestyle in order to minimize your risk of disease. The Story of Nic Volker Whole genome sequencing is becoming a new way to diagnose diseases or disorders that were undiagnosed using traditional tests. One miraculous example of this is the story of Nic Volker. Nic was a 6-year-old with a mysterious disease that caused many misdiagnoses and ineffective treatments. Eventually, researchers at the Medical College of Wisconsin used whole genome sequencing and diagnosed a rare genetic disease. This discovery is what saved his life. What is whole genome sequencing? Your genome is the unique blueprint for your body. Sometimes, because of new or inherited genetic mutations, your genes can cause a disease or increase your risk for disease. By sequencing your genome, health professionals can look at the unique variations found in your genes. Some of it matters. Some is still unknown or uncertain. It is most often used in medical research and is beginning to be used more in clinical practice. For example, a doctor or genetic counselor could use whole genome sequencing to see if a patient has a genetic disorder or is at risk for a disease. Whole genome sequencing results can be placed into 3 categories: Single- gene disorders, multi-factorial disorders, and the pharmacogenomic profile. Single-gene disorders sometimes also called Mendelian disorders are diseases that are caused by a mutation in the DNA for one gene. An example of these diseases is Sickle Cell Anemia. This often includes diseases like obesity and diabetes and often is highly influenced by your environment. This is an example of personalized medicine. How can I be tested? Today, whole genome sequencing is mainly used in research, but there are several companies that can sequence your DNA. These are known as direct-to-consumer tests. The testing that is offered through a physician is currently several thousand dollars. If you do choose to have your whole genome sequenced, it is very important and helpful to review your results with a trained professional. Also, you should make sure the lab is CLIA certified. What do the test results mean? Whole genome sequencing is not your average diagnostic test. Understanding disease risk from whole genomic sequencing Weather forecasting tries to predict what the weather will be like in an hour, a day, or a week. It involves knowledge of patterns and statistics. We then take that information and prepare for it by changing our plans or carrying an umbrella with us. Whole genome sequencing is a lot like weather forecasting. This means that it will tell you more about your risk for a certain disease, like diabetes, not if you have diabetes or not. We can take that information and change our lifestyle choices to better our health. Questions to consider Whole genome sequencing may not be right for everyone, so it is important to ask yourself whether you think it is right for you. Some may not want to know about their genetic risks whereas other people want to know everything about their genome. Here are some questions to think about if you are considering whole genome sequencing: Am I concerned about the privacy of my results? Who would I want to share my results with? How would I feel about sharing them with my employer or insurance company? How old should a person be before he or she can get tested? What will my results mean for my family members who may share a similar genetic makeup? Is there any information about disease risk that I would not want to know? Do I want to know about something that may not affect me in the next 10 or more years? Do I want to know about a genetic disease for which there is no treatment? What is my family history? Am I prepared to receive news that is unexpected? What would this information mean for my health? What sorts of actions would I take? Because the results of a genomic test are complicated and include a large amount of information, it is best to meet with a genetic counselor or trained health professional to explain your results and answer any questions or concerns you might have.

Chapter 5 : Microsoft Research â€“ Emerging Technology, Computer, and Software Research

Introduction. Software Testing is the process of executing a program or system with the intent of finding errors. Or, it involves any activity aimed at evaluating an attribute or capability of a program or system and determining that it meets its required results.

The first whole genome to be sequenced was of the bacterium Haemophilus influenzae. The worm Caenorhabditis elegans was the first animal to have its whole genome sequenced. Arabidopsis thaliana was the first plant genome sequenced. The genome of the lab mouse Mus musculus was published in It took 10 years and 50 scientists spanning the globe to sequence the genome of Elaeis guineensis oil palm. This genome was particularly difficult to sequence because it had many repeated sequences which are difficult to organise. The shift to more rapid, automated sequencing methods in the s finally allowed for sequencing of whole genomes. The first multicellular eukaryote, and animal , to have its whole genome sequenced was the nematode worm: Caenorhabditis elegans in Such samples may include saliva , epithelial cells , bone marrow , hair as long as the hair contains a hair follicle , seeds , plant leaves, or anything else that has DNA-containing cells. The genome sequence of a single cell selected from a mixed population of cells can be determined using techniques of single cell genome sequencing. This has important advantages in environmental microbiology in cases where a single cell of a particular microorganism species can be isolated from a mixed population by microscopy on the basis of its morphological or other distinguishing characteristics. In such cases the normally necessary steps of isolation and growth of the organism in culture may be omitted, thus allowing the sequencing of a much greater spectrum of organism genomes. Such capillary sequencers automated the early efforts of sequencing genomes. Sequencing of nearly an entire human genome was first accomplished in partly through the use of shotgun sequencing technology. While full genome shotgun sequencing for small â€” base pair genomes was already in use in , [27] broader application benefited from pairwise end sequencing, known colloquially as double-barrel shotgun sequencing. As sequencing projects began to take on longer and more complicated genomes, multiple groups began to realize that useful information could be obtained by sequencing both ends of a fragment of DNA. Although sequencing both ends of the same fragment and keeping track of the paired data was more cumbersome than sequencing a single end of two distinct fragments, the knowledge that the two sequences were oriented in opposite directions and were about the length of a fragment apart from each other was valuable in reconstructing the sequence of the original target fragment. The first published description of the use of paired ends was in as part of the sequencing of the human HPRT locus, [28] although the use of paired ends was limited to closing gaps after the application of a traditional shotgun sequencing approach. The first theoretical description of a pure pairwise end sequencing strategy, assuming fragments of constant length, was in The strategy was subsequently adopted by The Institute for Genomic Research TIGR to sequence the entire genome of the bacterium Haemophilus influenzae in , [31] and then by Celera Genomics to sequence the entire fruit fly genome in , [32] and subsequently the entire human genome. DNA Sequencing While capillary sequencing was the first approach to successfully sequence a nearly full human genome, it is still too expensive and takes too long for commercial purposes. Since capillary sequencing has been progressively displaced by high-throughput formerly "next-generation" sequencing technologies such as Illumina dye sequencing , pyrosequencing , and SMRT sequencing. Other technologies are emerging, including nanopore technology. Though nanopore sequencing technology is still being refined, its portability and potential capability of generating long reads are of relevance to whole-genome sequencing applications. However, further analysis must be performed to provide the biological or medical meaning of this sequence, such as how this knowledge can be used to help prevent disease. Methods for analysing sequencing data are being developed and refined. Because sequencing generates a lot of data for example, there are approximately six billion base pairs in each human diploid genome , its output is stored electronically and requires a large amount of computing power and storage capacity. While analysis of WGS data can be slow, it is possible to speed up this step by using dedicated hardware. Because of this, full genome sequencing is considered a disruptive innovation to the DNA array

markets as the accuracy of both range from The mutation frequency in the whole genome between generations for humans parent to child is about 70 new mutations per generation. In the specifically protein coding regions of the human genome, it is estimated that there are about 0. The distribution of somatic mutations across the human genome is very uneven, [81] such that the gene-rich, early-replicating regions receive fewer mutations than gene-poor, late-replicating heterochromatin, likely due to differential DNA repair activity.

Chapter 6 : Computer Based Testing Application Process

Application of genome and exome sequencing in the field of cancer research for companion diagnostics and biomarker development are expected to contribute towards the growth of this market throughout the forecast period.

This is hardly a matter of surprise when one considers that they both share many of the same objectives, techniques and application areas. Most of the O. During the next thirty or so years the pace of development of fundamentally new O. However, there has been a rapid expansion in 1 the breadth of problem areas to which O. Today, operations research is a mature, well-developed field with a sophisticated array of techniques that are used routinely to solve problems in a wide range of application areas. This chapter will provide an overview of O. A brief review of its historical origins is first provided. This is followed by a detailed discussion of the basic philosophy behind O. Broadly speaking, an O. The emphasis of this chapter is on the first and third steps. The second step typically involves specific methodologies or techniques, which could be quite sophisticated and require significant mathematical development. Several important methods are overviewed elsewhere in this handbook. The reader who has an interest in learning more about these topics is referred to one of the many excellent texts on O. The impetus for its origin was the development of radar defense systems for the Royal Air Force, and the first recorded use of the term Operations Research is attributed to a British Air Ministry official named A. Rowe who constituted teams to do "operational researches" on the communication system and the control room at a British radar station. The studies had to do with improving the operational efficiency of systems an objective which is still one of the cornerstones of modern O. This new approach of picking an "operational" system and conducting "research" on how to make it run more efficiently soon started to expand into other arenas of the war. Perhaps the most famous of the groups involved in this effort was the one led by a physicist named P. Blackett which included physiologists, mathematicians, astrophysicists, and even a surveyor. This multifunctional team focus of an operations research project group is one that has carried forward to this day. Its first presence in the U. Like Blackett in Britain, Morse is widely regarded as the "father" of O. These ranged from short-term problems such as scheduling and inventory control to long-term problems such as strategic planning and resource allocation. George Dantzig, who in developed the simplex algorithm for Linear Programming LP , provided the single most important impetus for this growth. To this day, LP remains one of the most widely used of all O. The second major impetus for the growth of O. The simplex method was implemented on a computer for the first time in , and by such implementations could solve problems with about constraints. Today, implementations on powerful workstations can routinely solve problems with hundreds of thousands of variables and constraints. Moreover, the large volumes of data required for such problems can be stored and manipulated very efficiently. Once the simplex method had been invented and used, the development of other methods followed at a rapid pace. The next twenty years witnessed the development of most of the O. The scientists who developed these methods came from many fields, most notably mathematics, engineering and economics. It is interesting that the theoretical bases for many of these techniques had been known for years, e. However, the period from to was when these were formally unified into what is considered the standard toolkit for an operations research analyst and successfully applied to problems of industrial significance. The following section describes the approach taken by operations research in order to solve problems and explores how all of these methodologies fit into the O. A common misconception held by many is that O. While it is true that it uses a variety of mathematical techniques, operations research has a much broader scope. It is in fact a systematic approach to solving problems, which uses one or more analytical tools in the process of analysis. Perhaps the single biggest problem with O. This is an unfortunate consequence of the fact that the name that A. Rowe is credited with first assigning to the field was somehow never altered to something that is more indicative of the things that O. Compounding this issue is the fact that there is no clear consensus on a formal definition for O. Churchman who is considered one of the pioneers of O. This is indeed a rather comprehensive definition, but there are many others who tend to go over to the other extreme and define operations research to be that which operations researchers do a definition that seems to be most often

attributed to E. Regardless of the exact words used, it is probably safe to say that the moniker "operations research" is here to stay and it is therefore important to understand that in essence, O. The key here is that O. One should thus view O. However, the final decision is always left to the human being who has knowledge that cannot be exactly quantified, and who can temper the results of the analysis to arrive at a sensible decision. To achieve this, the so-called O. This approach comprises the following seven sequential steps: Tying each of these steps together is a mechanism for continuous feedback; Figure 1 shows this schematically. The Operations Research Approach While most of the academic emphasis has been on Steps 4, 5 and 6, the reader should bear in mind the fact that the other steps are equally important from a practical perspective. Indeed, insufficient attention to these steps has been the reason why O. Each of these steps is now discussed in further detail. To illustrate how the steps might be applied, consider a typical scenario where a manufacturing company is planning production for the upcoming month. The company makes use of numerous resources such as labor, production machinery, raw materials, capital, data processing, storage space, and material handling equipment to make a number of different products which compete for these resources. The products have differing profit margins and require different amounts of each resource. Many of the resources are limited in their availability. Additionally, there are other complicating factors such as uncertainty in the demand for the products, random machine breakdowns, and union agreements that restrict how the labor force can be used. As an illustration of how one might conduct an operations research study to address this situation, consider a highly simplified instance of a production planning problem where there are two main product lines widgets and gizmos, say and three major limiting resources A, B and C, say for which each of the products compete. Each product requires varying amounts of each of the resources and the company incurs different costs labor, raw materials etc. The objective of the O. The first step in the O. The primary objective of this step is to constitute the team that will address the problem at hand and ensure that all its members have a clear picture of the relevant issues. It is worth noting that a distinguishing characteristic of any O. To digress slightly, it is also interesting that in recent years a great deal has been written and said about the benefits of project teams and that almost any industrial project today is conducted by multi-functional teams. Even in engineering education, teamwork has become an essential ingredient of the material that is taught to students and almost all academic engineering programs require team projects of their students. The team approach of O. Typically, the team will have a leader and be constituted of members from various functional areas or departments that will be affected by or have an effect upon the problem at hand. In the orientation phase, the team typically meets several times to discuss all of the issues involved and to arrive at a focus on the critical ones. This phase also involves a study of documents and literature relevant to the problem in order to determine if others have encountered the same or similar problem in the past, and if so, to determine and evaluate what was done to address the problem. This is a point that often tends to be ignored, but in order to get a timely solution it is critical that one does not reinvent the wheel. The aim of the orientation phase is to obtain a clear understanding of the problem and its relationship to different operational aspects of the system, and to arrive at a consensus on what should be the primary focus of the project. In addition, the team should also have an appreciation for what if anything has been done elsewhere to solve the same or similar problem. In our hypothetical production planning example, the project team might comprise members from engineering to provide information about the process and technology used for production , production planning to provide information on machining times, labor, inventory and other resources , sales and marketing to provide input on demand for the products , accounting to provide information on costs and revenues , and information systems to provide computerized data. Of course, industrial engineers work in all of these areas. In addition, the team might also have shopfloor personnel such as a foreman or a shift supervisor and would probably be led by a mid-level manager who has relationships with several of the functional areas listed above. At the end of the orientation phase, the team might decide that its specific objective is to maximize profits from its two products over the next month. It may also specify additional things that are desirable, such as some minimum inventory levels for the two products at the beginning of the next month, stable workforce levels, or some desired level of machine utilization. This is the second, and in a significant number of cases, the most difficult step of the O. The objective here is to further refine the deliberations from the orientation phase to the point where there is a

clear definition of the problem in terms of its scope and the results desired. This phase should not be confused with the previous one since it is much more focused and goal oriented; however, a clear orientation aids immeasurably in obtaining this focus. Most practicing industrial engineers can relate to this distinction and the difficulty in moving from general goals such "increasing productivity" or "reducing quality problems" to more specific, well-defined objectives that will aid in meeting these goals. A clear definition of the problem has three broad components to it. The first is the statement of an unambiguous objective. Along with a specification of the objective it is also important to define its scope, i. While a complete system level solution is always desirable, this may often be unrealistic when the system is very large or complex and in many cases one must then focus on a portion of the system that can be effectively isolated and analyzed. In such instances it is important to keep in mind that the scope of the solutions derived will also be bounded. Some examples of appropriate objectives might be 1 "to maximize profits over the next quarter from the sales of our products," 2 "to minimize the average downtime at workcenter X," 3 "to minimize total production costs at Plant Y," or 4 "to minimize the average number of late shipments per month to customers. These must further be classified into alternative courses of action that are under the control of the decision maker and uncontrollable factors over which he or she has no control. For example, in a production environment, the planned production rates can be controlled but the actual market demand may be unpredictable although it may be possible to scientifically forecast these with reasonable accuracy. The idea here is to form a comprehensive list of all the alternative actions that can be taken by the decision maker and that will then have an effect on the stated objective. The third and final component of problem definition is a specification of the constraints on the courses of action, i. As an example, in a production environment, the availability of resources may set limits on what levels of production can be achieved. This is one activity where the multifunctional team focus of O. In general, it is a good idea to start with a long list of all possible constraints and then narrow this down to the ones that clearly have an effect on the courses of action that can be selected. The aim is to be comprehensive yet parsimonious when specifying constraints. Continuing with our hypothetical illustration, the objective might be to maximize profits from the sales of the two products. The alternative courses of action would be the quantities of each product to produce next month, and the alternatives might be constrained by the fact that the amounts of each of the three resources required to meet the planned production must not exceed the expected availability of these resources.

Chapter 7 : Whole Genome Sequencing | Genes in Life

The Clinomics Program quickly moves discoveries from the research lab to the clinical setting, with practical, cost-efficient genomic tests for diagnosing and treating patients. Give Hope The Center for Individualized Medicine is a strategic priority for the Campaign for Mayo Clinic.

These diseases are most often caused by very rare genetic variants that are only present in a tiny number of individuals; [2] by contrast, techniques such as SNP arrays can only detect shared genetic variants that are common to many individuals in the wider population. In the past, clinical genetic tests were chosen based on the clinical presentation of the patient i. Target-enrichment strategies[edit] Target-enrichment methods allow one to selectively capture genomic regions of interest from a DNA sample prior to sequencing. Several target-enrichment strategies have been developed since the original description of the direct genomic selection DGS method in Twist Bioscience recently introduced Human Core Exome Enrichment Kit that enables researchers to perform more efficient capture of exomes than any other available method resulting in more complete enrichment of target sequences and lower sequencing depth requirements. Microarrays contain single-stranded oligonucleotides with sequences from the human genome to tile the region of interest fixed to the surface. Genomic DNA is sheared to form double-stranded fragments. The fragments undergo end-repair to produce blunt ends and adaptors with universal priming sequences are added. These fragments are hybridized to oligos on the microarray. Unhybridized fragments are washed away and the desired fragments are eluted. The fragments are then amplified using PCR. They developed the Sequence Capture Human Exome 2. The Agilent Capture Array and the comparative genomic hybridization array are other methods that can be used for hybrid capture of target sequences. Limitations in this technique include the need for expensive hardware as well as a relatively large amount of DNA. The probes labeled with beads selectively hybridize to the genomic regions of interest after which the beads now including the DNA fragments of interest can be pulled down and washed to clear excess material. The beads are then removed and the genomic fragments can be sequenced allowing for selective DNA sequencing of genomic regions e. This method was developed to improve on the hybridization capture target-enrichment method. In solution capture as opposed to hybrid capture, there is an excess of probes to target regions of interest over the amount of template required. The preferred method is dependent on several factors including: Sequencing[edit] Main article: Comparison with other technologies[edit] There are multiple technologies available that identify genetic variants. Each technology has advantages and disadvantages in terms of technical and financial factors. Two such technologies are microarrays and whole-genome sequencing. Microarray-based genotyping[edit] Microarrays use hybridization probes to test the prevalence of known DNA sequences, thus they cannot be used to identify unexpected genetic changes. Although exome sequencing is more expensive than hybridization-based technologies on a per-sample basis, its cost has been decreasing due to the falling cost and increased throughput of whole genome sequencing. It is not able to identify the structural and non-coding variants associated with the disease, which can be found using other methods such as whole genome sequencing. Presently, whole genome sequencing is rarely practical in the clinical context due to the high costs and time associated with sequencing full genomes. Exome sequencing allows sequencing of portions of the genome over at least 20 times as many samples compared to whole genome sequencing, at the same cost. Even by only sequencing the exomes of individuals, a large quantity of data and sequence information is generated which requires a significant amount of data analysis. Challenges associated with the analysis of this data include changes in programs used to align and assemble sequence reads. False positive and false negative findings are associated with genomic resequencing approaches and is a critical issue. A few strategies have been developed to improve the quality of exome data such as: Comparing the genetic variants identified between sequencing and array-based genotyping [1] Comparing the coding SNPs to a whole genome sequenced individual with the disorder [1] Comparing the coding SNPs with Sanger sequencing of HapMap individuals [1] Rare recessive disorders would not have single nucleotide polymorphisms SNPs in public databases such as dbSNP. More common recessive phenotypes may have disease-causing variants reported in

dbSNP. Screening out such variants might erroneously exclude such genes from consideration. Genes for recessive disorders are usually easier to identify than dominant disorders because the genes are less likely to have more than one rare nonsynonymous variant. Using lists of common variation from a study exome or genome-wide sequenced individual would be more reliable. A challenge in this approach is that as the number of exomes sequenced increases, dbSNP will also increase in the number of uncommon variants. It will be necessary to develop thresholds to define the common variants that are unlikely to be associated with a disease phenotype. Of course, it is possible to reduce the stringency of the thresholds in the presence of heterogeneity and ethnicity, however this will reduce the power to detect variants as well. Using a genotype-first approach to identify candidate genes might also offer a solution to overcome these limitations. Ethical implications[edit] New technologies in genomics have changed the way researchers approach both basic and translational research. With approaches such as exome sequencing, it is possible to significantly enhance the data generated from individual genomes which has put forth a series of questions on how to deal with the vast amount of information. Should the individuals in these studies be allowed to have access to their sequencing information? Should this information be shared with insurance companies? This data can lead to unexpected findings and complicate clinical utility and patient benefit. This area of genomics still remains a challenge and researchers are looking into how to address these questions. This additional depth makes exome sequencing well suited to several applications that need reliable variant calls. Rare variant mapping in complex disorders[edit] Current association studies have focused on common variation across the genome, as these are the easiest to identify with our current assays. However, disease-causing variants of large effect have been found to lie within exomes in candidate gene studies, and because of negative selection , are found in much lower allele frequencies and may remain untyped in current standard genotyping assays. Whole genome sequencing is a potential method to assay novel variant across the genome. However, in complex disorders such as autism , a large number of genes are thought to be associated with disease risk. This sample size issue is alleviated by the development of novel advanced analytic methods, which effectively map disease genes despite the genetic mutations are rare at variant level. Exome sequencing in rare variant gene discovery remains a very active and ongoing area of research: Discovery of Mendelian disorders[edit] This section does not cite any sources. Please help improve this section by adding citations to reliable sources. Unsourced material may be challenged and removed. December Learn how and when to remove this template message In Mendelian disorders of large effect, findings thus far suggest one or a very small number of variants within coding genes underlie the entire condition. Because of the severity of these disorders, the few causal variants are presumed to be extremely rare or novel in the population, and would be missed by any standard genotyping assay. Exome sequencing provides high coverage variant calls across coding regions, which are needed to separate true variants from noise. A successful model of Mendelian gene discovery involves the discovery of de novo variants using trio sequencing, where parents and proband are genotyped. Case studies[edit] A study published in September discussed a proof of concept experiment to determine if it was possible to identify causal genetic variants using exome sequencing. After exclusion of common variants, the authors were able to identify MYH3 , which confirms that exome sequencing can be used to identify causal variants of rare disorders. Subsequently, another group reported successful clinical diagnosis of a suspected Bartter syndrome patient of Turkish origin. Exome sequencing revealed an unexpected well-conserved recessive mutation in a gene called SLC26A3 which is associated with congenital chloride diarrhea CLD. This molecular diagnosis of CLD was confirmed by the referring clinician. This example provided proof of concept of the use of whole-exome sequencing as a clinical tool in evaluation of patients with undiagnosed genetic illnesses. This report is regarded as the first application of next generation sequencing technology for molecular diagnosis of a patient. A second report was conducted on exome sequencing of individuals with a mendelian disorder known as Miller syndrome MIM , a rare disorder of autosomal recessive inheritance. Two siblings and two unrelated individuals with Miller syndrome were studied. They looked at variants that have the potential to be pathogenic such as non-synonymous mutations, splice acceptor and donor sites and short coding insertions or deletions. Previous exome sequencing studies of common single nucleotide polymorphisms SNPs in public SNP databases were used to further exclude candidate genes. After exclusion of these genes, the authors found

mutations in DHODH that were shared among individuals with Miller syndrome. Each individual with Miller syndrome was a compound heterozygote for the DHODH mutations which were inherited as each parent of an affected individual was found to be a carrier. This exciting finding demonstrates that exome sequencing has the potential to locate causative genes in complex diseases, which previously has not been possible due to limitations in traditional methods. Targeted capture and massively parallel sequencing represents a cost-effective, reproducible and robust strategy with high sensitivity and specificity to detect variants causing protein-coding changes in individual human genomes. Clinical diagnostics[edit] Exome sequencing can be used to diagnose the genetic cause of disease in a patient. Identification of the underlying disease gene mutation s can have major implications for diagnostic and therapeutic approaches, can guide prediction of disease natural history, and makes it possible to test at-risk family members. The first time this strategy was performed successfully in the clinic was in the treatment of an infant with inflammatory bowel disease. Analysis of exome sequencing data identified a mutation in the XIAP gene. Our results demonstrate that this technology will be particularly valuable for gene discovery in those conditions in which mapping has been confounded by locus heterogeneity and uncertainty about the boundaries of diagnostic classification, pointing to a bright future for its broad application to medicine". Personal genomics Multiple companies have offered exome sequencing to consumers. Knome was the first company to offer exome sequencing services to consumers[when? The company provided raw data, and did not offer analysis.

Chapter 8 : Exome sequencing - Wikipedia

F-test for testing significance of regression is used to test the significance of the regression model. The appropriateness of the multiple regression model as a whole can be tested by this test. A significant F value indicates a linear relationship between Y and at least one of the Xs.

Support Our Vision Clinomics Program In the not-so-distant future, whole-genome sequencing â€" determining your entire unique DNA makeup in the laboratory â€" will be as routine as X-rays and cholesterol testing. The challenge, though, is in the accurate interpretation of the vast amount of data generated by genomic sequencing and effectively using it to guide decisions about your health care. Improving patient care by turning genomic research into real-world personalized medicine applications, particularly new and better genomics-based diagnostic tests, is the goal of the Clinomics Program. With these new tests in hand, your doctor will be able to quickly and effectively search your genetic code for clues that help him or her diagnose and optimally treat your condition â€" or keep you healthy by preventing future disease. The Clinomics Program includes the Individualized Medicine Clinic, ongoing translational research projects and a request for application RFA program for advancing the science. The RFA program funds next-generation sequencing and early-stage bioinformatics services for Mayo Clinic investigators who are conducting clinical studies and research projects. Individualized Medicine Clinic Currently, the Individualized Medicine Clinic uses whole-exome sequencing to make diagnoses and recommend appropriate treatments for patients. We take a team approach in the clinic, with physicians, genetic counselors, laboratorians, bioinformaticians and bioethicists working together to solve certain types of extremely challenging cases. The Individualized Medicine Clinic today offers two services for patients: This service is for patients with advanced cancer who have exhausted all treatment options that have proven survival benefits. Whole-exome sequencing of their normal DNA and tumor DNA may be used to identify genetic alterations mutations that are causing or expanding the cancer. This information is then used to find available treatments that can target those mutations. Rare and undiagnosed diseases. This service is for patients who have a possible genetic condition and have undergone previous single-gene based genetic testing, but still have not received a clear diagnosis. These patients are sometimes known as "diagnostic odyssey" cases. This includes patients with an early-onset disease or a syndromic disease of unknown etiology, as well as those whose family history suggests their condition is inherited. Whole-exome sequencing may be used to discover the genetic alterations that contribute to disease development or might influence treatment. Projects Hereditary Colon Cancer Test The Clinomics Program, along with the Department of Laboratory Medicine and Pathology, has developed a comprehensive diagnostic panel of 17 hereditary colon cancer genes using next-generation sequencing technologies. For the first time, clinicians can now order a single test when pursuing a diagnosis of hereditary colon cancer. Previously, Mayo Clinic ran individual tests for the five genes most frequently mutated in hereditary colorectal cancer cases. Other genes known or suspected to play a role in the disease could be tested by various labs around the world, but nowhere comprehensively. The new hereditary colon cancer test has a cost comparable to ordering just three independent DNA sequencing assays using standard technologies. Whole-exome Sequencing Data Analysis Many questions remain about how whole-exome sequencing are best used in patient care. To begin answering them, we have been conducting many projects that analyze whole-exome sequencing data from Mayo Clinic Biobank samples. As is being shown through care in the Individualized Medicine Clinic, analysis of these data will continue to improve how we: Determine which variants and findings are clinically relevant and actionable Share results concisely and effectively with clinicians and patients Address bioethical considerations as they arise The data are also being used to compare different genomics sequencing approaches and determine which are most suitable for clinical applications.

Chapter 9 : Usability Testing of Icons

Whole genome sequencing (also known as WGS, full genome sequencing, complete genome sequencing, or entire

genome sequencing) is ostensibly the process of determining the complete DNA sequence of an organism's genome at a single time.