requires signals generated from interaction of the T-cell receptor with the processed antigenic peptide on the major histocompatibility complex (MHC) molecule, and also co-stimulatory signals and regulatory cytokines [e.g. interleukin 12 (IL-12)] from the antigen-presenting cells (APCs). This APC response can be induced by pathogen molecules (e.g. lipopolysaccharide, bacterial DNA and viral RNA) interacting with pattern-recognition receptors, including toll-like receptors on macrophages and dendritic cells. However, activation of innate cells with a range of pathogen molecules from a virus or bacteria can also induce pro-inflammatory cytokines, such as IL-1β, that lead to local and systemic reactogenicity, fever and neurological effects [6]. Therefore, the aim is to present the foreign antigen in a vector, adjuvant or inert vaccine delivery system, that will activate the innate, and hence the adaptive, immune response in a way that will not induce excessive inflammation. Some of the viral vectors under development have good safety profiles in clinical trials, but immune responses to the inserted heterologous antigens have not always been that spectacular.

Other problems, such as the limit imposed on repeated use because of immunity to the vector, can, in theory, be overcome by switching vectors for the booster doses. However, such problems still put vectors at a disadvantage over naked DNA or the purified recombinant vaccines. By contrast, major advantages of the live virus vector over the purified recombinant approach are that the antigen is replicating and that it is presented to the immune system in its native conformation. Because the antigen is synthesized in the host, it will be properly folded and glycosylated, and can gain entry to the endogenous route of antigen processing in the APCs, thus allowing induction of functionally important antibodies and class I-restricted T cells, respectively. The big question is whether it will be possible to generate persistent immunity to the heterologous antigen in humans using live vectors, without the potential problems associated with actively replicating viruses, especially in immunocompromised individuals. The answers should come from understanding the immunology of the problem and using molecular biology to design the solution.

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Want novel drugs in a hurry? You had better do the math!

The recent article in *Drug Discovery Today* entitled 'Prioritizing the proteome: identifying pharmaceutically relevant targets' by Swindells and Overington [1] focuses our attention on a new dynamic that promises to reshape the drug discovery process. In essence, the article highlights the increasing importance of complex and computationally demanding data-mining processes that are needed to extract information and knowledge from ever-larger and more-diverse data sets.

Consider, for example, that a typical protein structure takes 3–10 megabytes of storage. Multiply this by the 100,000 or more proteins thought to comprise the human proteome. Add to this the hundreds of thousands of corresponding protein structures from the pharmacological model species (dog, rat, mouse and primates), or to the hundreds of thousands, potentially millions, of protein structures from the various genomic model species, as well as the entire spectrum of infectious disease agents. This just begins to define the challenge, as well as the opportunity, posed by the massive influx of data from a growing arsenal of modern drug discovery tools [2]. Gene-expression array data, large-scale proteomics analyses, high-throughput small-molecule screening (each molecule potentially characterized by hundreds of descriptors), broad-spectrum clinical laboratory data or adverse drug reaction data generated through multi-test panels for thousands of clinical trial subjects or patients – each of these tools or data sources contains a wealth of information that today remains largely invisible or inaccessible.

The data sets generated by these new tools are often large in magnitude, sparse, noisy and multi-dimensional. In addition, they often afford only a well-buried, weak signal. Extracting information and knowledge from such data poses large computational and information-storage challenges. IBM's rapidly growing and highly successful commercial commitment to life science applications appears to be well thought out (not unexpectedly), and confirms the recognition of this important growing need. The complementary and

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vital challenge is, of course, the creation of mathematical algorithms capable of handling this type of data. Here, we enter the domain of mathematicians and physicists who focus daily on exactly the same mathematical challenges, albeit in entirely unrelated fields. Perhaps the best example is that of aerospace- and defence-related data analysis. For example, hyperspectral data from imaging satellites are large in magnitude, sparse, noisy and multi-dimensional, with weak, well-buried signals [3]. Here, the successful and robust application of pattern-recognition and data-fusion technologies to extract information quickly is not only an everyday occurrence, but sometimes even a matter of life or death.

Swindells and Overington have done an excellent job in defining the mathematical challenges faced in identifying drug targets based upon analysis of sequence and 3D structural information. Their observation that the 'best results' for prioritizing the proteome will probably come from the interplay between experimental and computational methods is, I think, a fundamental insight. The iteration of experiment and computation applies equally well to many aspects of drug discovery research, and particularly to the new and data-prolific tools mentioned above.

The take-home lesson is that the flood of new experimental tools that is producing miraculous amounts of data, imposes an unambiguous requirement for increasingly sophisticated mathematical analysis. For companies that fail to do the math, the numbers might just not add up.

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A new era as plate movers get on track

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The second meeting of the *European Laboratory Robotics Interest Group* (ELRIG; http://www.lab-robotics.org/Europe/) was held at the Sanger Centre (http://www.sanger.ac.uk) on 2 May 2002. ELRIG is the European chapter of the Laboratory Robotics Interest Group, which aims to facilitate the free exchange of information between users and providers of laboratory automation. The meeting, subtitled *Plate Movers – Getting the Arm on the Right Track,* was attended by over 400 delegates and included scientist- and vendor-based talk sessions and a 25 vendor exhibition, showcasing everything from bench-top robotics to industrial automation. The inaugural meeting of ELRIG, *Liquid Handling*, was held in November 2001.

New solutions in plate moving

The first session of the day was chaired by John Major (Head of HTS at AstraZeneca's UK Alderley Park site; http://www.astrazeneca.com) and detailed some of the novel technologies for the manipulation of microplates of all types.

Paul Lomax from Perkin Elmer Life Sciences (http://www.perkinelmer.com) compared modular workstations with integrated systems and discussed the benefits of having conveyors, arms or both. The Minitrak™ series was mentioned, which is capable of manipulating 96-, 384- and 1536-well plates. Removable stackers and shuttle mechanisms for plate movements were also described. Advantages of the modular system are that it is high speed and reliable but limitations are that it requires manual scheduling and plate transfer. Integration options include pipetters and grippers of third party devices via the 'diving board' placed on either end of the track.

On a similar track, Simon Sheard (RTS Life Sciences; http://www.rts-group.com/life-science/) described the various options in microplate manipulation. These options include converges, sliders, static robots and track systems. The vision of the future is to be able to pick a single colony or a particular cell of interest. He described the cell culture systems acCellerator™ and AssayPlatform™ and how independent technologies need to be adapted to each particular laboratory, be cost effective, reliable, robust and appropriate to the experiment at hand.

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