Hello and welcome to the first edition of the bimonthly STIMulus Newsletter. STIM (Students for Technology In Medicine) is a new student interest group dedicated to all things tech in medicine. One of our primary goals is to educate ourselves and our peers about all the latest and greatest happenings in the world of medical bio-tech, and come together to discuss the incredible advances that are shaping the future of our profession.

Here, we present a distillation of a fraction of a portion of just some of the things that are happening in science and engineering in medicine. We live in a time where technological advances regularly transform previously impossible musings into milestones of the past, and we should be a part of that. The more we collectively know, and are able to articulate, the more we can work together with the interdisciplinary groups that design the future of medicine. We hope this newsletter inspires you to learn more. We hope you join us in bringing more information to the table. The stronger these collaborations, the better off our field and our patients will be.

STIMulus is open to anybody who would like to submit an article. We are looking for any article on new tech, new procedures, faculty spotlights and interviews, opinion pieces on the ethics of controversial technology applications, reviews, etc. We all have a unique background and are capable of contributing a valuable voice to the collective discussion. We hope that you take the time to investigate our newsletter, and let us all know what kind of exciting things are out there. We look forward to reading your submissions.

Sincerely,

Katelyn Gurley
Vikramjeet Singh
Co-Founders of STIM
Visions of the Future: The US Healthcare of Tomorrow

Tony Tzeng

Introduction

Walking into a present-day hospital, a physician from the early 20th century would find himself immersed in a nearly unrecognizable environment. Advances in technology and research in the sciences have facilitated unprecedented progress in medicine. Within the last century, doctors have improved their understanding of disease pathologies and mechanisms, conquering various medical challenges and saving countless lives. Discoveries and inventions like vaccinations and antibiotics have transformed healthcare in the United States.

Despite these advances, troubling discontinuities remain in the healthcare system: patient dissatisfaction escalates as costs continue to skyrocket. This cost inflation has not correlated with corresponding improvements in the quality of care; in recent years, US healthcare has fared sub-optimally compared to its international counterparts1. As patient demand rises from an influx of baby boomers presenting with chronic comorbidities, the increased patient volume and complexity further exacerbates issues faced by medicine today.

Upgrading Our Tools

Just as universal healthcare tools, like the stethoscope, have evolved through the decades, current technologies will also transform. Particular healthcare technologies that will be enhanced include those involved in healthcare delivery, continuation of care, and patient education and empowerment. Ranging from diagnostic modalities to electronic health records (EHRs) to patient educational multimedia, these technologies will be shaped by the pressures and challenges of the current environment.

One major factor affecting health outcomes is improved diagnostic technologies that facilitate earlier disease detection. Radiographic imaging and sequencing have vastly upgraded the diagnostic capabilities physicians have at their disposal. Since their introduction, these technologies continue to be refined. Radiography, including MRI and PET scans, has developed better specificity, sensitivity, and molecular imaging capabilities that can be utilized in tracking disease biomarkers. Similarly, other diagnostic tools, such as sequencing and assays, have become more efficient, characterizing and identifying pathogenic organisms in an increasingly timely manner. These tests can now also detect resistance profiles, which will play a vital role in treatment plans, especially in this era of widespread antibiotic resistance. These innovative capabilities need to be incorporated into the standard of care and will further enhance healthcare delivery.

EHRs currently facilitate the transfer of patient information between physicians, ensuring continuity of care, but complaints from physicians include incessant pop-up alerts and non-intuitive systems that force them to spend more time in front of a computer than interacting with patients. However, the future could see a universal and more user-friendly system with enough flexibility for general practitioners and specialists. Such systems could become more adaptive in warning of potential adverse events, minimizing false positive alerts. EHRs should and will enhance the physician-patient relationship rather than obstruct it: EHRs of the future will improve continuity of care between all providers and enhance healthcare delivery integration and coordination of care.

As more patients present with multiple comorbidities, the patient’s role in medicine has evolved, shifting from medical paternalism to active patient participation. Beyond receiving health information solely in the physician’s office, patients now have access to such information with a single click; furthermore, multimedia has been harnessed to enable and encourage the patient to stay informed about their own health. Currently, smart phone apps can not only provide scientifically valid information and reminders for daily medications but...
can, with input devices, measure glucose levels or record electrocardiograms, alerting the patient of impending medical crises. In the future, these applications can be improved, validated, and expanded to measure a plethora of critical health markers. Ubiquitous smart devices will become key tools for empowered healthcare, especially for patients at high risk of adverse events. Actively engaged patients will work together with physicians, enhancing healthcare delivery, decreasing overall health costs, and most importantly, optimizing patient satisfaction.

Glimpses into the Future

Many new ideas and innovations, while currently in their infancy, could revolutionize physicians’ abilities to deliver patient care. Advances in nanotechnology will yield therapeutics of unprecedented precision, with nanoparticles capable of delivering payloads ranging from anti-cancer drugs to small molecule RNA\(^2\). Stem cell research could transform the lives of patients affected by currently untreatable conditions: curing hearing loss or reversing neuro-degeneration through regulated cellular regeneration is potentially within reach\(^3,4\). Gene therapy, temporally and spatially controlled through radio waves, magnetic fields, or light, may allow precise modification of gene expression with outcomes such as the activation of insulin expression in diabetics or the restoration of sight compromised by retinal diseases\(^5,6\). Finally, the proverbial Damocles’ sword, antibiotics resistance, seemed posed to apocalyptically reverse the major gains of the 20\(^{th}\) and 21\(^{st}\) centuries. But with the first significant antibiotic discovery in decades, teixobactin, and the development of a novel method of cultivating and utilizing the vast arsenal of microorganisms incapable of growing in a petri dish, the fight against antibiotic resistance no longer appears as bleak\(^7\). This cutting edge technique could provide a wealth of possibilities, not just for new antibiotics but also for new therapeutics against other diseases like cancer. Finally, progress has been made in alleviating the debilitating effects of mental disorders, which bear the further burden of societal stigma. A greater understanding and acceptance of mental health in the future will lead to other therapeutics that avoid the pitfalls of current ones, such as significant side effects and varying effectiveness depending on dosage and individual\(^8,9,10\).

Conclusion

The keys for the future lie in better organized and coordinated medical care, continued research of disease processes and treatments, and increased focus on patient education and involvement. Advances in novel technologies and treatments are promising, with great potential on numerous fronts against varying diseases. However, as the internet and other sources continue to bombard patients with information, it is crucial for physicians to provide accurate information through the use of these same media and to challenge false assertions made by well-intentioned but misguided sources. Although medicine faces several challenges, the progress of medical development is and will continue to be miraculous: no doubt the present-day physician will be astounded should he or she wander through the hospital wards of the next century.

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5 Apple Apps that Patients Could Be Using Right Now:

1) **GlucoSuccess** (by the Massachusetts General Hospital) – Keeps track of glucose levels by syncing to the glucometer

2) **Asthma Health** (by Mount Sinai) – Monitors local air quality and reminds patients of their medications

3) **Parkinson mPower Study app** – Monitors Parkinson symptoms (speech, gait, finger tapping, and memory) over time using iPhone sensors

4) **Share the Journey** – Another symptom tracker for patients after breast cancer treatment

5) **MyHeart Counts** (by Stanford University) – Tracks fitness and educates patients on their own heart conditions
The birth of the earliest prototypes of 3D printers was in the late 1980s, but it has been gaining popularity recently, especially in the healthcare field. 3D printing works similarly to an inkjet printer: a head or needle moves back and forth in a predetermined pattern and squirts material along the way. In the case of an inkjet printer, it’s ink. In the case of a 3D printer, it’s plastic, silicone, or even cellular material. With the growing availability of 3D printing, doctors are finding ways that it can help their practice. For instance in the cardiovascular surgery field, there have been doctors from New York, Kentucky, and Florida who have created 3D printed replicas of their patient’s hearts to help plan for a complicated surgery.

Conventionally, doctors would open the chest, stop the heart, look inside, and figure out what to do. By utilizing modern technology, these doctors decided to use 2D slices from either CT or MRI scans to create a computerized 3D model and print out a model of the diseased hearts. From here, they were able to manipulate vessels, peer into chambers, and create plans to redirect blood flow or remove obstructions. Even more, their patients have had accelerated post-surgery recovery times when compared to patients who have been treated using conventional methods.

3D printing is also benefiting surgeons-in-training. At Nottingham Trent University in London, a man named Richard Arm claims that he has a model of a human heart that is “as close as you can get without creating artificial muscle fibres.” He uses CT scans to determine the densities of the different parts of the heart and then uses a blend of different silicone gels to print a squishy, true-to-color human heart. He claims that it is so realistic a surgeon trainee could cut into it and it would be not unlike cutting into a real heart. By utilizing 3D printing instead of working on basic plastic models, students will have a chance to experience the sensation of cutting into a heart and practice without repercussions. The university also plans on pumping artificial blood through the heart to produce an even more realistic simulation.

Perhaps the most attractive possibility of 3D printing is that of creating human organs. Scientists have already succeeded in creating a phenotypically functioning liver (although it was 500 microns thick and lived only five days). Some experts suggest that a 3D printed heart is not far off: perhaps within ten years! This could solve numerous problems. Some patients may not be candidates to receive from an organ donor, and, of course, some may not find a suitable match in time. If constructed from the patient’s own cells, rejection and anti-rejection drugs wouldn’t be an issue.

Stuart K Williams, executive and scientific director at the Cardiovascular Innovation Institute at the University of Louisville, has some lofty goals. His vision is for the patient to enter the operating room, have some fat tissue removed, isolate stem cells, mix those cells with extracellular matrix materials, and print the heart within hours. However, today’s 3D printing timescales are more along the lines of an overnight process and are still being refined.

As with any endeavor in new realms of medicine, these types of advances in biotechnology require inter-professional alliances. Engineers need to collaborate with physiologists to create a mechanically and electrophysiologically functioning heart, and engineers need clinicians to access patients who need these technologies. Do you think you have what it takes to venture to the forefront of medical technology? LSUHSC School of Medicine’s Learning Center has their very own 3D printer: a Makerbot Replicator Z18. Consider working with the Learning Center on ideas or projects that could potentially help future patients!
Valvular heart disease can lead to very serious complications and is a leading cause of morbidity and mortality in aging populations. An estimated 67,500 surgical aortic valve replacements are performed annually in the United States\(^1\), and with an aging population, the demand for such surgical intervention will only increase.

Mechanical prosthetics can be used to replace failing valves, but they can also lead to complications resulting from clotting and scarring. Additionally, as these prosthetics are non-living, they are unable to perform dynamic remodeling in response to mechanical stress, and can wear out over time\(^2\). A common approach is to replace a failing valve with one from an animal heart of similar size (usually porcine or bovine), a procedure known as a xenograft. However, biologic valves are susceptible to fibrosis and calcification, and can lead to immunogenic rejection of the graft causing heart failure\(^3\).

In the past several years, biomedical engineers have worked towards a more elegant approach, in which a patient’s own cells are used to grow a living replacement heart valve. The approach uses biological scaffolds, a three-dimensional fiber skeleton suspended in a hydrogel upon which autologous stem cells can proliferate and develop\(^4\). The scaffold, made of synthetic polymer or de-cellularized animal/donor tissue, mimics the extracellular material of a native valve (a mixture of collagen, elastin, and glycosaminoglycans), providing the tissue with its structural support. Scaffolds are then permeated with developing autologous cells, which can be found in the endothelial cells of peripheral arteries, or in bone marrow derived stem cells\(^5\). The structure is placed in a biomimetic environment, and the scaffold provides support until sufficient new tissue forms, as the scaffold eventually degrades.

This approach to growing allograft transplants addresses many of the problems associated with mechanical or biological valves, particularly in mitigating the immune response to foreign tissue. Furthermore, the scaffold approach provides a living tissue that exhibits remodeling, regeneration, and growth potential\(^6\), and also reduces blood damage from mechanical trauma as it is grown specifically to operate within a physiological system.

Living tissue engineered heart valves have shown success implanted in animal models, with adequate functionality for an extended time\(^7\). The technique shows great promise for the future of cardiovascular repair; however, there is more to learn about the exact biochemical processes which facilitate neotissue remodeling. With greater understanding, a more intelligent design can be implemented, perhaps incorporating specific signaling molecules into the scaffold to obtain a safe, durable, and precisely designed end product. As the technique is refined, the possibility for more complex organ synthesis could become a real possibility, giving hope to those waiting for new parts.

**FUN FACT:** Arne Larsson was the first patient to receive an implantable pacemaker and outlived the inventor and the surgeon.
Cardiac Arrest: Back to the Basics in the Out of Hospital Setting

Tony Tzeng

At the front lines of medical care, every minute is crucial, and every decision could mean the difference between life and death. Emergency medical service (EMS) personnel operating in non-hospital environments must stabilize and transport the patient rapidly, often in suboptimal conditions. These personnel, including paramedics, are often trained not only in basic life support (BLS), which includes ventilation, cardiopulmonary resuscitation, and AED defibrillation, but also in more complex advanced life support (ALS) procedures such as advanced airway and intubation techniques. However, current findings question the effectiveness of ALS compared to BLS procedures with recent studies suggesting a lack of significantly superior outcomes from ALS in the majority of trauma and non-traumatic situations.

Cardiac arrest, particularly in the out of hospital setting, remains a significant problem in the United States as well as internationally despite improvements in survival rates. In fact, statistics from the American Heart Association (AHA) suggests that 359,000 cases of out of hospital cardiac arrest occur annually in the United States. However, studies suggest a lack of evidenced-based support for improved outcomes from ALS compared to BLS treatment in cardiac arrest patients in the non-hospital, non-traumatic setting. This article will review the current literature concerning ALS versus BLS techniques in out of hospital cardiac arrests.

In the first study comparing ALS and BLS utilizing a United States population, Sanghavi et al found that BLS had an overall lower charge per survivors to one year, and BLS treated patients had better outcomes. Patients had higher rates of surviving to hospital discharge and 90 days and improved neurological functionality. These results are similar to results from international studies by Ma et al and Stiell et al, suggesting that BLS is superior in care and transport of out-of-hospital cardiac arrest.

The benefits of ALS are advanced airway techniques and IV drug delivery yet scant evidence supports the assumption that these techniques lead to improvements in patient care. Endotracheal intubation and supraglottic airway devices are the most common advanced airway techniques utilized by paramedics. Studies, including a notable study by Hasegawa et al, suggest that in comparison to bag mask ventilation, intubation results in poorer outcomes and survival to discharge in out-of-hospital cardiac arrest. A recent systematic review incorporating 17 observational studies has also found worse outcomes from supraglottic airways compared to intubations. Overall in the study, there were superior outcomes from basic airway interventions over advanced airway techniques, including both intubation and supraglottic airways.

Several possibilities may explain this discrepancy in ALS and BLS care in out-of-hospital cardiac arrest patients. Causes of this decline in patient outcomes from advanced airway techniques may be attributed to the risks of unrecognized intubation of the esophagus, exacerbation of original injuries, and hindrance of chest compressions as well as insufficient training and practice. As noted in previous studies, significant experience with intubation is necessary for successful placement—over 100 intubations are needed for a 95% success rate in the ideal surgical hospital environment —so it is not wholly unexpected that emergency personnel, in suboptimal conditions with a much lower proficiency and practice rate have substandard patient outcomes with this technique.

The second benefit of utilizing ALS is IV drug delivery. However, IV drug administration of agents like epinephrine did not have a profound effect on long term outcomes after a year though some studies did find immediate short term effects on survival leading to and up to one month following discharge. Further complicating analysis of the effects of IV drug administration is the widespread variation in drug administration by EMS personnel in the United States, which may contribute to the lack of effectiveness of ALS interventions.
Lastly, time also may be a crucial factor causing the differing outcomes in ALS and BLS techniques, with Sanghavi et al reporting longer times on scene by ALS personnel which may delay transport to the hospital and have adverse effects on outcomes\textsuperscript{10}.

However, it would remiss not to consider confounding factors and weaknesses in the literature. Crucially, the majority of these studies were observational studies, especially since a randomized control trial may be challenging to conduct in these circumstances. (Con’t) Therefore, the result is that the effects of biases and confounding factors are much greater. Perhaps the most difficult to account in this situation would be the bias of indication: a patient who is indicated for an out of hospital intubation may have worse outcomes regardless of which techniques were utilized. Additionally, procedures in EMS systems may vary greatly geographically in the United States such as regarding drug administration, let alone internationally, suggesting that studies from abroad may be less applicable to the situation in the US. Finally, most if not all of these studies were conducted in an urban environment, and their results and conclusions may not necessarily be as relevant in a rural environment since transport time as well as access to medical care and resources may be different than in a city.

In conclusion, ALS procedures either need to be improved or de-emphasized in favor of the BLS techniques in out of hospital cardiac arrest patients. Health policy and procedures need to reflect the literature in order to best optimize the care given to these patients, a population who already has a high mortality rate. Overall, this review demonstrates the importance and need for relying on evidence-based medicine in patient care.
What if you could predict a major outbreak before it happened? Imagine building vaccines for pathogens that have years of evolution left before they are able to cause disease. As technology continues to develop at an exponential pace, such possibilities have already been introduced to the realm of reality. Instead of mere speculation, researchers today are able to predict the evolution of asexual organisms such as viruses or cancer cells with an algorithm-based approach to evolution developed by researchers at the Max Planck Institute for Developmental Biology in Tübingen in Germany. This algorithm was first tested in the development of a vaccine for the A/H3N2 influenza virus for the 2015 flu season.

The thinking behind this algorithm references the branches of the genealogical trees of an organism to infer the capability of the organism to survive. The driving idea is that the fitter lineages have more offspring. Thus, the genealogical trees of these lineages will have more branches. Previously, fitness models have been developed using surface proteins, as well as amino acid sequences, to predict seasonal influenza viruses; however, such fitness models are extremely difficult to develop for most organisms. The beauty of using this new general algorithmic approach is that it relies on no molecular data pertaining to viruses whatsoever. Instead, the algorithm infers fitness from the shape of the genealogical trees derived from historical data. Since many offspring implies high fitness, the shape of the genealogical tree is used as a marker for high fitness. The algorithm requires a genealogical tree as input; a tree can be reconstructed from a sample of genomic sequences. The algorithm then traces fitness along lineages and integrates across the tree to deliver a quantitative result. Hence, the method builds upon our increasing understanding of the statistical structure of genealogies in adapting populations to construct a quantitative model of fitness dynamics. There are two key assumptions the researchers used in developing this method. The first is that the populations are constantly undergoing directional selection. Second, small effect mutations accumulate throughout lineages to affect overall fitness dynamics.

For validation and reliability purposes, the researchers tested this algorithm-based method on both simulated data and historical data on seasonal A/H3N2 virus sequences occurring in North America and Asia from 1995 to 2013. For testing purposes, the researchers used genetic data of viral surface proteins from one year to reconstruct a genealogical tree. This tree was then used as input in the algorithm to predict the dominant viral strain type for the upcoming year. The results showed that for the majority of the 19 years analyzed, the method gave informative predictions regarding the viral type that would be prevalent in the upcoming year. When compared with a model designed specifically for influenza using genetic data, the genealogical tree based algorithm made predictions of similar reliability while retaining the capability of being applied to many different organisms not just influenza.

This methodology makes a lot of sense in the world of quantitative data analysis. It is proof of concept that simple algorithms such as the one described can be used to make precise assessments of future outcomes that can be applied to different organisms without the need to develop complex models based on explicit data. From a statistical standpoint, correcting for predicted vs attained changes and integrating data from a number of years can lead to the development of more precise algorithms that are essential for developing technology based approaches to healthcare and medicine.
WE LOVE FEEDBACK! Should we add medical technology puns? How about funny pictures? What other topics should we include? Let us know how we’re doing! We are completely open to suggestions and ideas. Most importantly, we want to know what YOU, our readers, think!

Have a professor you really want to interview? Read an article you think will benefit your peers? Have an opinion on technology you want heard? Email us with your article today!

Our next deadline for the April/May edition is April 24th

Students for Technology In Medicine (STIM) is a student-run organization of the LSU Health Sciences School of Medicine with a focus on providing educational and networking opportunities for students who are interested in the field of biotechnology as it relates to the field of medicine. We hope to raise community awareness of the local, regional, and global technological advancements and bioinnovations that will be crucial in future patient healthcare.

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Fun Fact


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