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The Capacious and the Ambiguous in Biomolecular Engineering

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Abstract

The significant clinical potential of biomedical endeavors provided by the functionings of biomolecular engineering can be illuminated especially vividly when utilizing various derivations of nucleic acid-based biological techniques, nanoparticles, and nanostructured dendrimers. Nucleic acids are capable of high-performance operation in genetic pathways and living systems at large in the form of tractable devices. Nanoparticles offer versatility in synthetic design. Dendrimers allow for biomaterial conjugations that can precisely transport drugs and kill targeted tumor cells. And especially when accompanied by specified conceptualizations of cell growth and drug delivery, these seismic areas of innovation demonstrate striking medical relevancy and immediacy. Imbued with an ethos of vertical integration, biotechnological interventions of the body will tend to establish bodies of medical knowledge at every scale and stage of diagnosis. The trajectory of biomolecular engineering will, however, need to address more social or humanistic complications related to the interstitial history of ethical transgression in the technological development of medicine.

Introduction

The development and manufacturing of biotechnology at a molecular scale has great potential for improving human health and well-being. For instance, by regulating and mitigating harmful genes or increasing the efficiency and accuracy of drug delivery mechanisms, many avenues for treatment are opened. Promoting stem cell differentiation and other forms of cell growth and differentiation repairs damaged cells, tissues, and even entire organisms (Vigneshvar, Sudhakumari, Senthilkumaran, & Prakash, 2016). Precise engineering design models are necessary for developing the nanodevices and nanodevice systems so essential to the nanotechnological innovation that contributes to the wide-ranging functionality of molecular engineering. These models take into account the intricate geometries of the biomaterials in question (at the molecular, cellular, and tissue-based scales) (Hu, Fine, Tasciotti, Bouamrani, & Ferrari, 2011). Modalities of sensing and imaging—how signals from alterations on biomaterials transmit information related to the shape and movement of the biomaterials providing the mechanical input—can contribute to effective biological innovation (Berezin & Achilefu, 2010). A particular system of feedback (reception, recognition, and response) that characterizes the dynamics of a certain cellular activity often involves the pathways of flowing biochemical signals and proteins instrumental to cell communication. Analyzing such cascades, together with studying the effects shape manipulations (mechanical changes observed within biological space, whether triggered by natural processes or artificial inputs) have on the function of different synthesized (by engineers) as well as indigenous biological structures, can illustrate a series of cause and effect relationships. These relationships mark the target "area" of a technological apparatus applied to a living system (Mehrotra, 2016). These "measurements" serve as, in effect, parameters for such technologies, indicating to specific devices and machines the exact biomechanical and biochemical pathways to induce (by activating the right proteins and signals).

Nucleic Acid Molecular Engineering

The nanoscale bioengineering of nucleic acids has the concrete capacity to reshape the processes by which we conceptualize human biology, providing the creative space needed for a proliferation of clinical possibilities. Modernized biochemical methodologies allow for the collection of a massive range of nucleic acids in high purity (Simmel, 2007). The base pairings of nucleotides Guanine and Cytosine, together with the matching of Adenine with Thymine (DNA) or Uracil (RNA), forms the code of nucleic acids. The fact that these combinations are easily interpreted and malleable to computational mechanisms has generated the formation of richly diverse nucleic acid-based nanodevices (Krishnan & Simmel, 2011). Because of their organic, shared genealogies with living systems (including shared origins and molecular composition),

these fabricated nucleic acid-based devices have massive advantages in their ability to interplay with those living systems (Michelotti, Johnson-Buck, Manzo, & Walter, 2012). Crucially, the chemical qualities of nucleic acids themselves provide generous efficiencies to building scaffolds of nucleic acids. Interfacing these nanoscale structures with biological processes is a task fundamental to the future of biotechnology (Garmann et al., 2015).

The structural intricacies of nucleic acid formations and the functionings they underpin are incredibly valuable for the bioengineering of programmable and productive manufactured biological devices (Shlyahovsky, Li, Lioubashevski, Elbaz, & Willner, 2009). Naturally-occurring nucleic acid-based devices, like riboswitches, messenger RNA molecules that can regulate the translation of genetic data used to produce protein (other messenger RNAs enact the translation), can be almost entirely made up of RNA (Breaker, 2012). Another natural RNA device, MicroRNA (miRNA), similarly regulates gene expression by repressing RNA translation (MacFarlane & Murphy, 2010). MiRNAs are themselves tightly managed, enlisting a regime of maintenance so potentially unstable that irregularities in this management is cause for disease (MacFarlane & Murphy, 2010). Another issue has to do with the life-cycle of miRNA itself, as some types of pre-miRNA are configured in structures with mechanical blockages sprouting from inefficiencies in protein recognition that prevent these antecedents from developing into fully-formed miRNA (Kang, 2011).

Nanoparticles

Nanoparticles can go a long way in addressing some of these inadequacies. As inorganic particles under a hundred nanometers in size, they allow for a variety of properties important for biological engineering. The binding and solubility of these particles in chemical reactions in large part depend upon surface coatings, and at smaller scales the surface area of a particle increases relative to mass. Because this widens the mathematical basis for using nanoparticles as functional, interactive participants in biomechanical and biochemical pathways, combining and calibrating the advantageous tendencies of nanoparticles and biomaterials holds great promise for the development of synthetic biological units.

Proteins and nucleic acids can be integrated in order to create biological systems that approximate the real-life biology of living organisms in the rigorous accuracy of their manufactured processes (Wang & Wang, 2014). Nanoparticles, because they are generated outside living systems, can broaden the horizons of biological system design (in terms of the fabrication, consolidation, and operation of composite biomaterials) (Hu et al., 2015). They can also act as catalysts to capture the benefits of the more particular and environmentally contingent qualities of given biomolecules.

One example involves ASODN (antisense oligodeoxynucleotides)

nucleotides (the building blocks of nucleic acids) and RNase H, an enzyme capable of targeted nucleotide degradation. These two molecules can be conjugated and functionalized together on magnetic nanoparticles (magnetic properties making up a subset of the conveniences of inorganic material) (Watts & Corey, 2011). The conjugation substrate (magnetic nanoparticles) must be incubated in order to establish linkages by modifying the amino groups (Nitrogen atoms bound to Hydrogen atoms) on the nanoparticles. This modification is made in accordance with the connective orientation of the amino groups of ASODN and RNase H, respectively. The products are nanoparticles with the technical biological ability to not only survey and spur the processing of targeted RNA but also dispose of unwanted targeted RNA sequences (Watts & Corey, 2011).

The hybridization of ASODN and RNase H multiplies the possible utilizations of their individual qualities to stringently regulate the expression of various genes (Michelotti et al., 2012). It is precisely in this sense that magnetic nanoparticles conjugated with ASODN and RNase H show promise in the targeted degradation of given nucleic acids. Such a process might take the appearance of an ASODN attached to the nanoparticle, "luring" targeted RNA and conjugating with it while the nearby RNase H digests the targeted RNA into smaller units (Watts & Corey, 2011).

The regulation of gene expression in protein synthesis processes is one beneficial application of nanoparticles. Protein synthesis reactions activated by the superfolder green fluorescent protein (sfGFP) gene can be blocked by the introduction of nanoparticles carrying ASODN and RNase H. The RNase H digests the mRNA sequence which translates the genetic information into the protein, thereby preventing synthesis of this protein (Lee et al., 2016). Because this ASODN-RNase H conjugation was assisted by the weak and ephemeral magnetic properties of the underlying nanoparticle (given the corollary ease of amino group modification needed to link with ASODN and RNase H) (Watts & Corey, 2011), a lack of magnetic attractions inactivates the ASOND-RNase H system and allows the original protein synthesis reaction to continue (Shlyahovsky et al., 2009). The direct result of this biophysical feature is that introducing and removing the nanoparticle or sets of nanoparticles is a method of rapidly turning protein synthesis "on" or "off" (Lee et al., 2016).

The fundamental adaptability of nanoparticles in their engagement with biomaterials is authentically conducive to the creative and diagnostic imperatives of synthetic biology. Nanoparticles can deepen understandings of molecular pathways in their constructive interferences with natural and artificial molecular machines.

Dendrimers

Dendrimers are highly branched, versatile nanostructures first synthesized by scientists in 1978 (Verlag, 1978). A vast range of design strategies are made possible by their unique interior and surface shape configurations.

The variation in the size of cavities within the internal core creates adaptability in a dendrimer's absorption capacity, just as variant chemical bonding on a dendrimer's surface determines the degree of solubility (which in turn determines how and which biomaterials will be captured, transported, and released). Operating as nanocontainers, dendrimers enlist the services of receptor proteins working inside a biochemical signaling pathway in order to bind to target molecules (Abbasi et al., 2014). Structurally, the dendrimer carrier as well as the molecular "package" remain intact and embedded within a larger matrix of biomechanical and biochemical signaling. Target biomaterials are searched, attached, and sent to a target location and/or to another target molecule. Essentially, biomechanical properties embed them within the wide world of possibilities of medical nanoengineering. Targeted biological imaging and drug-delivery are among the clinical fields most subject to this arena of innovation (Madaan, Kumar, Poonia, Lather, & Pandita, 2014).

Mechanisms for the synthesizing of an especially versatile polyamidoamine dendrimer prototype have earned substantial scholarly attention for over a decade (Wang, Brechbiel, & Wiener, 2003). Qualities and tendencies of such a structure allow for effective, diagnostic MRI (magnetic resonance imaging), use as clear contrast agents, and for biomolecule delivery (Kobayashi & Brechbiel, 2003). Current research focuses on first identifying protein-ligand interactions and then applying demdrimers to improve delivery of drugs to the specific cells that express that protein.

When a number of ligands find multiple points of access and bind at the same moment in time to multiple receptors located on given biological surfaces, the detection and imaging of a range of targeted cell types can be improved (Salakhieva et al., 2016). Manufactured biological apparatuses often employ these multivalent affinities because multifocal binding has been demonstrated to generate a great degree of avidity (attraction) between the ligand and the receptor protein (Madaan et al., 2014). Effector molecules can be the ligands to bind onto the receptor proteins. They can act as inhibitors which block functional pathways and immobilize proteins by attaching to non-active allosteric regions of the receptor. These effectors tend to show higher levels of ligand-protein attraction compared to similarly synthesized effectors which instead attach to active sites on the protein. This, in turn, engenders the relevant biological functional pathways and allows the systems of feedback regulation to proceed (Yu, Tai, Xue, Lee & Lee, 2010).

The particular identification and directing of molecular therapies to cancerous cells is an optimal treatment strategy, shown to better address, contain, and/or avoid any toxicity (Madaan et al., 2014). Here, we will focus on cancer drug delivery via folic acid receptors. The overexpression of these receptors in epithelial cancer cells was discovered and used as a method of drug delivery. This method was then improved by the introduction of a dendrimer scaffold, serving as a prime example of how

biomolecular engineering capitalizes on existing biological systems. Folic acid is attracted to the folate receptor, whose protein is often overexpressed up to one hundred-fold in epithelial (referring to tissue linings in organs and blood vessels) cancer cells (like those involved in breast, lung, and brain cancers), and folic acid and folate receptors form folic acid complexes. Many folic acid complexes are proficient in molecular targeting to tumors (Zhang et al., 2010). These folate receptor proteins are expressed on the regions of cells facing interstitial tissue, rather than on the interior-facing surfaces where normal expression takes place. It is precisely this proximity to blood that allows folic acid, when active as a tracking vessel, to have an astute, biomedically conducive awareness of the particularities of cancer cells (Zhang et al., 2010). Folic acid is minuscule enough to easily find its way inside tumors and is hardly expensive, so it has experienced broad popularity in biochemical recognitions and analysis and in biological tracking (Mishra et al., 2011). Protein-based toxins, liposomes enveloped in drugs, and many types of nanoparticles are some common targets of folic acid (Mishra et al., 2011).

One complication of targeting mechanisms predicated on folate molecules by themselves is that they have levels of affinity constrained by folate quantity (many are needed for adequate affinity). In more problematic scenarios, the circumscribed attraction of folate targeting materials even bounded the outputs of drug delivery to an extent dreadfully inadequate for cancer cell therapeutics (Majoros, Myc, Thomas, Mehta, & Baker, 2006).

Biomolecular engineers sought to improve this system of drug delivery by incorporating dendrimers into the system. Experimental analysis of a drug delivery device based on a polyamidoamine scaffold, branched to multiple folic acid molecules, within *in vivo* contexts, has made apparent the advantages of this nanostructured device transporting drugs as opposed to the folic acid molecules themselves operating individually and freely (Madaan et al., 2014). The most plausible reason for folate acid molecules working through the scaffold being more effective than those operating independently is the multiplicity and high level of attraction of the interplay taking place across the folic acid groups externally on the dendrimer (Patri, Majoros, & Baker, 2002). Dendrimer scaffolds branched to folic acid molecules were quantitatively tested in response and resulted in a strength of ligand-protein (in this case, surface folate binding proteins) binding (important for efficiency and continuity in therapeutic drug delivery) in the weakest regions of at least 2,000 times as strong as individual folic acid molecules (Kang, 2011).

Collections of such experimental data vindicate the capacity of polyamidoamine dendrimer scaffolds to function in multivalent binding systems. Quantitatively, there was a positive, linear relationship between the association constant (representing binding strength) and the number of targeting vessels involved (demonstrating its value as an explanatory variable) (Patri et al., 2002). In other words, the more the polyamidoamine

dendrimers are branched, the more targeting molecules (in this case, folic acid) they contain, and the higher the affinity between the ligand and the receptor. In this way, the targeting and tracking mechanism is streamlined.

Polyamidoamine dendrimers are key to the development of expansive, multipurpose cancer-therapy nanostructured devices. It is important, then, that there are several modifications that can improve the effectiveness of these dendrimers. Adding a partial acetyl group to the dendrimer allows for the neutralization and containment of some of the negative effects caused by amino groups comprising the dendrimer. Such a measure also increases solubility (important for binding), and prevents unintended, overly broad and promiscuous detection and targeting over the course of drug transport (Majoros et al., 2006). Amino groupings without the added acetyl group can still be helpful in combining folic acid (again, important because it targets the folate receptor proteins), drugs like methotrexate, and contrast agents needed for clear imaging (Majoros et al., 2006).

Methotrexate, a drug commonly conjugated to folic acid (which has long been suspected of being able to neutralize some of the harmful side effects of methotrexate, as a "folate antagonist") is a chemotherapeutic drug often applied to forms of cancer (Thomas et al., 2005) and arthritis (Weinblatt, 2013). The DNA replication of cancerous cells that enables the overexpression of folate receptors relies on the dihydrofolate reductase enzyme, which is blocked by methotrexate. Folic acid binds to these overexpressed receptors, and the dendrimer delivers methotrexate to those cells. It is in this way that the overexpressed receptor-expressing cancer cells are killed (Zhang et al., 2010). Thereby, the folic acid-methotrexate device is adept in accurately tracking and degrading these cancer cells through their relationship with excessively expressed, yet fully-formed, folate receptor proteins (Quintana et al., 2002).

Here, Quintana et al. summarize their work on the folic acid receptor drug delivery system:

> The cellular uptake and cytotoxicity of an engineered multifunctional dendritic nanodevice containing folic acid (FA) as the targeting molecule, methotrexate (MTX) as the chemotherapeutic drug, and fluorescein (FI) as the detecting agent were studied in vitro.
> Methods: The device is based on an ethylenediamine core polyamidoamine dendrimer of generation 5. Folic acid, fluorescein, and methotrexate were covalently attached to the surface to provide targeting, imaging, and intracellular drug delivery capabilities. Molecular modeling determined the optimal dendrimer surface modification for the function of the device and suggested a surface modification that improved targeting.
> Results: Three nanodevices were synthesized. Experimental targeting data in KB cells [a tumor cell] confirmed the modeling predictions of specific and highly selective binding. Targeted delivery improved the cytotoxic response of the cells to methotrexate 100-fold over free drug.
> Conclusions: These results demonstrate the ability to design and produce polymer-based nanodevices for the intracellular targeting of drugs, imaging agents, and other materials (Quintana et al., 2002)

This multifunctional dendrimer-based device can be abbreviated as

G5-FI-FA-MTX. The G5-FI-FA-MTX conjugated product activated molecular pathways that lead to the inhibition of cell growth in KB tumor cells, because the capacity of G5-FI-FA-MTX nanodevices to detect, target, and finally repress the proliferation of cancerous cells directly derive from their folic acid component's affinity to overexpressed folate receptor proteins (Zhang et al., 2010).

Drugs primarily useful for cancer therapy traditionally are dangerous due to a lack of precision in toxicity. However, precise polymer-predicated targeting techniques tailored to cancer cells can bridge many of these biomolecular inadequacies (Madaan et al., 2014).

When fabricated to completion, these nanodevices are deeply effective, transporting chemotherapeutic drugs to specifically selected cancer cells. Manufacturing these devices at larger material scales and ensuring real-life clinical familiarity should follow.

Dendrimers are nanostructures, and drug delivery often encompasses the conceptual space of nanoengineering. A dexterity in working with transport systems inside of cells as well as with imaging methodologies for mapping the cellular uptake of the given transported biomaterials would allow nanodevices to carry out multi-purposed processes.

Polymers can be structurally altered in order to integrate biomaterials applicable to targeting endeavors. Sending the polymer directly to the tumor brings therapeutic drugs with the facility to destroy the tumor cells. As these combinations of polymers and cancer therapy drugs are made more accurate and specific in tracking cancerous cells and become embedded in more complex systems of device manufacture, toxicity is minimized and the most restorative characteristics of the drugs are highlighted (Madaan et al., 2014).

Polymeric drug conjugates have several advantages over free drugs, especially since they face decreased drug resistance (Patri et al., 2002). Several synthetic and natural polymers of this sort have been tested in the past decade for targeting tumor cells (Kang, 2011).

Ideally, drug delivery mechanisms specifically geared for tumor cells necessitate an apparatus advanced enough to contain a variety of functionally central parts, like therapeutic drugs and fluorescent sensors (Majoros et al., 2006). Polyamidoamine dendrimers can build such transport systems because of their well-defined branches, themselves containing (either within interior void space or by covalent bonding on their surface) a plethora of biomolecules (Zhang et al., 2010). And thinking beyond these particular tactics for drug delivery, dendrimers have been utilized for their carrying qualities in a wide spectrum of medical capacities, whether they are agents for delivering drugs, sharpening imaging, or outlining radioactive molecules (Abbasi et al., 2014).

Problematics

It is always paramount to consider the context in which we attain an understanding of and seek to apply bioengineering precepts and to grapple

with the sources and implications of our motivations in doing just that. When we map genetic pathways in order to devise new methodologies for genetic engineering, lineages of racialized eugenics must be confronted in deciding the ends of nucleic acid interventions. Is it only the diseases and disorders that scientists are motivated to influence, and how can engineers reconcile universalizing, uniform impulses of human health with the right of people excluded from hierarchies of mental as well as physical health and able-bodiedness to demand dignity and humanity? If the primary endgame is movement away from perceived imperfections, can the drivers of modern biological analysis articulate what they really imagine as ideal products of biomedicine, and how such centricities relate to larger inequity and marginalization in social relations?

What is the ethical value of, for instance, imposing on deaf children a lifestyle and single-mindedly concentrating resources for "curing" deafness and neglecting the potential technological ingenuities of, say, sign language and deaf culture in the hopes of them replicating mainstream society (Harris, 2016)? Instead of obsessively developing cochlear implants and promoting a clinical discourse that ostracizes the deaf as deviants (Harris, 2016), medical engineers and practitioners should provide the most precisely engineered tools for them to experience freedom and self-worth in whichever way they choose.

The same questions must be asked of biomolecular efforts of drug detection and pharmacological efforts towards cancer therapy. Which contestable ideologies and funding patterns influence the manners in which malignancies are interpreted and treated (and within these paradigms how can the interests of patients be held with the highest regard)? The constantly expanding collection of biological data obtained and maintained by modern bioengineering make our representations of living systems more lucid and are elemental to the extensive capacities of computational biology (Tyagi, Hopkins, Baker, Jordan, & Tang, 2015). But do the connections of bioinformatics and more general tensions between "Big Data" and structures of often discriminatory systems of surveillance and control figure into experimental investigations (DeAngelis, 2014; Hernandez, 2016)? Are they simply relegated to the realm of the abstract, to be dealt with after the fact? The internal conditions of human biology can be monitored at every moment of the day (DeAngelis, 2014), but where is the line between disease prevention through the ability to have specialized professionals *notified* of disturbances or irregularities (Institute of Medicine US Forum on Microbial Threats, 2007) and absolute, permanent violations of privacy for the *sake* of surveillance, of being an object of knowledge at all times, drawn?

No doubt, orienting the body as object enables access to information that can help the cause of that very body. But objectification also requires an exertion of power and holds a certain degree of freedom away from the object, the afflicted, not allowed to speak but only to exist (in the extreme

objectifying processes of human slavery, this contradiction is resolved by the infliction of "social death") (Patterson, 1982). And when these generations of selfhood and domination are symbiotically furthered by particularly pernicious power relations, the consequences of objectifying analysis are horrific.

Instructive is the following example: Saartjie Baartman, a South African Khoikhoi woman, whose body was toured around 19th Century European circuses; her particular body shape put forward as representing the 'essence' of all African women, and as an object of sick European fascination. Even in her death she was not spared the racialized misogyny of the European gaze; her brain, skeleton and sexual organs remained on display in a Paris museum until 1974, more than 150 years after her death in 1815 (Gebrial, 2017).

The narrative arc of biomedical study then is not simply an unrelenting march towards an improved understanding of human biology and refined clinical practice. Its methodology can be complicit in or even encourage regressive functions, like the inhumane imprisonment of those who dominant layers in society saw/see as mentally impaired based on psychiatric hypotheses and the means of psychiatric diagnosis (Metzner & Fellner, 2010). The histories are complicated and interwoven with human histories, not reducible to the cause of pragmatic scientific efficiency. Difficult questions cannot be separated from the interrogation and investigation of biological materials. Biological materials themselves must not be made to appear contained and isolated from the scrutiny of human realities.

Modern nanobiotechnology takes as its inspiration and foundation the historical phenomenon of technocratic medicine, and so its extension of the sphere of possible medical knowledge down to drastically small compartments is in many senses also a multiplication and division of sociality, technology, and the body. Fundamentally, nanoscale biomedicine as discourse is likewise woven together with a faith in the neutrality of empirically analyzing a clearly bounded human body. What tends not to be considered is the authoritarian potential of the epistemic asymmetry between doctor and patient and, now, engineer and social body. The terror made possible by this intimacy in situations of extreme disparity in agency is demonstrated in the restrictions of institutions of benevolent confinement (like the mental hospital) and has historical parallels with the institutional development of plantation slavery and the modern prison (Foucault, 1963/2003; Hartman, 2010).

But of course, a wholesale repudiation of the claims of modern nanotechnology, let alone the history of modern medicine, would also require its own discursive exclusions and its own complicity in coercions of thought. Human freedom and health, however produced conceptually and even materially in occluded subjugations and repressions, by no means should be abandoned; in fact, it is their very ambiguity and reflexivity that creates spaces of freedom (Butler, 2006). Biomolecular

engineering cannot possess a monopoly on this reflexivity, this multidimensionality. To maintain the conceptual integrity necessary to be an intelligible, recognizable, and applicable discipline, the preconditions, methodologies, and conclusions of biomolecular engineering must, as a matter of principle, cede ground to other sciences and currents of thought.

Conclusions

Creativity is found to be boundless in the fruitful dialogues of molecular engineering and nanotechnology with biological study. The corporeal subject is one that demands a unique academic and conjectural lens, due to the intense self-actualization it receives from us as human beings. As such, this is a circumstance that allows for a special degree of engineering imagination and exploration. Nucleic acid-centered devices, nanoparticles, and built dendrimer nanostructure-based devices provide a framework for powerful medical revolutions, literally expanding the realm of the possible. In addressing sources of human pain and trauma through drug delivery and cancer therapeutics, these techniques were outlined for what they can currently regard as victories and heroisms but also for what they ought to be able to do and what institutions and industries must be structurally calibrated to foster and consistently work towards. Models and design blueprints are needed more than ever to orient critical biomaterial geometries in promoting essentially humanist biotechnologies. Dramatically pioneering solutions for human problems of health and well-being can be the result.

It is by acknowledging and embracing the multidirectionality of biomedical engineering and its many currently existing layers (including biomolecular engineering) that the field can become authentically multidisciplinary. Even the languages used to describe our biology could be made more open-handed and sympathetic, thoroughly respectful of anybody that exists in an objectified relation to the subjective, investigative clinical eye. If biotechnologies are to be endlessly reshaped, let the essence of the science push these innovative processes to flow in multifaceted directions. Consistency with democratic modes and impressions of human advancement, rather than a search for a single, utopian totality, socially conditioned to reify some identities and acquisitions of knowledge and to discredit others, should be sought.

References

Abbasi, E., Aval, S. F., Akbarzadeh, A., Milani, M., Nasrabadi, H. T., Joo, S. W., ... Pashaei-Asl, R. (2014, May 21). "Dendrimers: Synthesis, Applications, and Properties." *Nanoscale Research Letters*. Springer. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4074873/

Butler, J. (2006) "The Psychic Life of Power: Theories in Subjection." *The Psychic Life of Power: Theories in Subjection* (pp. 10–20). Stanford: Stanford Univ. Press.

Berezin, M. Y., & Achilefu, S. (2010, May 12). "Fluorescence Lifetime Measurements and Biological Imaging." *Chemical Reviews*. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2924670/

Breaker, R. R. (2012, Feb.). "Riboswitches and the RNA World." *Cold Spring Harbor Perspectives in Biology*. Cold Spring Harbor Laboratory Press. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3281570/

DeAngelis, S. (2014) "Patient Monitoring, Big Data, and the Future of Healthcare." *Wired.com*. Conde Nast Digital. Retrieved from https://www.wired.com/insights/2014/08/patient-monitoring-big-data-future-healthcare/

Foucault, M. (2003) "The Birth of the Clinic." (Sheridan, A. M., Trans.). London: Routledge. (original work published 1963)

Garmann, R. F., Sportsman R., Beren C., Manoharan V. N., Knobler C. M., & Gelbart W. M. (2015, June 10). "A Simple RNA-DNA Scaffold Templates the Assembly of Monofunctional Virus-Like Particles." *National Center for Biotechnology Information*. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26043403

Gebrial, D. (2017, February 13). "Decolonising Desire: The Politics of Love." *Versobooks.com*. www.versobooks.com/blogs/3094-decolonising-desire-the-politics-of-love

Harris, M. (2016, June 08). "Do Deaf Babies Need to Be Fixed?" *Pacific Standard*. Retrieved from https://psmag.com/do-deaf-babies-need-to-be-fixed-20aa00d9446

Hartman, S. V. (2010) "Scenes of Subjection: Terror, Slavery, and Self-Making in Nineteenth-Century America." *Scenes of Subjection: Terror, Slavery, and Self-Making in Nineteenth-Century America*. New York, NY: Oxford University Press.

Hernandez, D. (2016, Jan. 11). "Big Data Healthcare: The Pros and Cons of Remote Patient Monitoring - MedCity News." *MedCity News*. Retrieved from http://medcitynews.com/2014/03/big-data-healthcare-pros-cons-remote-patient-monitoring/

Hu, Y., Fine, D. H., Tasciotti, E., Bouamrani, A., & Ferrari, M. (2011, Jan.). "Nanodevices in Diagnostics." *Wiley Interdisciplinary Reviews. Nanomedicine and Nanobiotechnology*. U.S. National Library of

Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2962874/

Institute of Medicine (US) Forum on Microbial Threats. (2007). "Summary and Assessment - Global Infectious Disease Surveillance and Detection - NCBI Bookshelf." *National Center for Biotechnology Information*. National Academy of Sciences. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK52862/

Kang, K. (2011). "MicroCantilever (MC) Based Nanomechanical Sensor for Detection of Molecular Interactions." *Iowa State University Digital Repository*. Iowa State University. Retrieved from http://lib.dr.iastate.edu/cgi/viewcontent.cgi?article=3145&context=etd

Kobayashi, H., & Brechbiel M. W. (2003, Jan.). "Dendrimer-based Macromolecular MRI Contrast Agents: Characteristics and Application." *National Center for Biotechnology Information*. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12926232

Krishnan, Y., & Simmel, F.C. (2011, Mar. 28). "Nucleic Acid Based Molecular Devices." *National Center for Biotechnology Information*. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/21432950

Lee, J.W., Kim, H. J., & Heo, K. (2015, Apr.). "Therapeutic Aptamers: Developmental Potential as Anticancer Drugs." *BMB Reports*. Korean Society for Biochemistry and Molecular Biology. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4436860/

Lee, K., Min, S., Kim, H. Lee, S., & Kim, D. (2016, Feb. 09). "A Molecular Nanodevice for Targeted Degradation of MRNA during Protein Synthesis." *Nature.com*. Nature Publishing Group. Retrieved from http://www.nature.com/articles/srep20733

MacFarlane, L., & Murphy, P. R. (2010, Nov.). "MicroRNA: Biogenesis, Function and Role in Cancer." *Current Genomics*. Bentham Science Publishers Ltd. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3048316/

Madaan, K., Kumar, S., Poonia, N., Lather, V., & Pandita, D. (2014). "Dendrimers in Drug Delivery and Targeting: Drug-dendrimer Interactions and Toxicity Issues." Journal of Pharmacy & Bioallied Sciences. Medknow Publications & Media Pvt Ltd. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4097927/

Majoros, I.J., Myc, A., Thomas, T., Mehta, C. B, & Baker, J. R. Jr. (2006, Feb.). "PAMAM Dendrimer-based Multifunctional Conjugate for Cancer Therapy: Synthesis, Characterization, and Functionality." National Center *for Biotechnology Information*. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16471932

Mehrotra, P. (2016, Jan. 06). "Biosensors and Their Applications – A Review." *Journal of Oral Biology and Craniofacial Research*. Elsevier. Retrieved from

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4862100/

Metzner, J. L., & Fellner, J. (2010, Mar. 01). "Solitary Confinement and Mental Illness in U.S. Prisons: A Challenge for Medical Ethics." *Journal of the American Academy of Psychiatry and Law*. Retrieved from *http://www.jaapl.org/content/38/1/104.full.pdf+html*

Michelotti, N., Johnson-Buck, A., Manzo, A. J., & Walter, N. G. (2012, Sept. 01). "Beyond DNA Origami: A Look on the Bright Future of Nucleic Acid Nanotechnology." *Wiley Interdisciplinary Reviews. Nanomedicine and Nanobiotechnology*. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3360889/

Mishra, M. K., Kotta, K., Hali, M., Wykes, S., Gerard, H. C., Hudson, A. P., … Kannan, R. M. (2011, May 19). "PAMAM Dendrimer-azithromycin Conjugate Nanodevices for the Treatment of Chlamydia Trachomatis Infections." National Center for Biotechnology Information. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/21658474

Patri, A. K., Majoros, I. J., & Baker, J. R. Jr. (2002) "Dendritic Polymer Macromolecular Carriers for Drug Delivery." *Current Opinion in Chemical Biology* (2002): 466-71. University of Michigan. Retrieved from http://www.nano.med.umich.edu/publications/Patri-2002-CurrOpChemBi.pdf

Patterson, O. (1982) "Slavery and Social Death a Comparative Study." Cambridge, MA: Harvard University Press.

Quintana, A., Raczka, E., Piehler, L., Lee, I., Myc, A., Majoros, I., … Baker, J. R. Jr. (2002, Sept.). "Design and Function of a Dendrimer-Based Therapeutic Nanodevice Targeted to Tumor Cells Through the Folate Receptor." SpringerLink. Retrieved from http://link.springer.com/article/10.1023/A:1020398624602

Salakhieva, D. V., Sadreev, I. I., Chen, M. Z. Q., Umezawa, Y., Evstifeev, A. I., Welsh, G. I., & Kotov, N. V. (2016, Apr. 18). "Kinetic Regulation of Multi-ligand Binding Proteins." *BMC Systems Biology*. BioMed Central. Retrieved from https://bmcsystbiol.biomedcentral.com/articles/10.1186/s12918-016-0277-0

Shlyahovsky, B., Li, Y., Lioubashevski, O., Elbaz, J., & Willner, I. (2009). "Logic Gates and Antisense DNA Devices Operating on a Translator Nucleic Acid Scaffold." *ACS Nano*. ACS Publications. Retrieved from http://pubs.acs.org/doi/abs/10.1021/nn900085x

Simmel, F. C. (2007, Dec.). "Towards Biomedical Applications for Nucleic Acid Nanodevices." *Future Medicine*. Retrieved from http://www.futuremedicine.com/doi/abs/10.2217/17435889.2.6.817

Thomas, T. P., Majoros, I. J., Kotlyar, A., Kukowska-Latallo, J. F., Bielinska, A., Myc, A., & Baker, J. R. Jr. (2005, June). "Targeting and Inhibition of Cell Growth by an Engineered Dendritic Nanodevice." *National Center for Biotechnology Information*. U.S.

National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/15916424

Tyagi, E., Hopkins, R. C., Baker, D., Jordan, K., & Tang, S. (2015). "Development of Genomic Surveillance Bioinformatics Modules." *Online Journal of Public Health Informatics*. University of Illinois at Chicago Library. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4512416/

Verlag, G. T. (1978) ""Cascade"- and "Nonskid-Chain-like" Syntheses of Molecular Cavity Topologies." *Synthesis* 02.

Vigneshvar, S., Sudhakumari, C. C., Senthilkumaran, B., & Prakash, H. (2016, Feb. 16) "Recent Advances in Biosensor Technology for Potential Applications– An Overview." *Frontiers in Bioengineering and Biotechnology*. Frontiers Media S.A. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4754454/

Wang, E. C., & Wang, A. Z. (2014, Jan.). "NANOPARTICLES AND THEIR APPLICATIONS IN CELL AND MOLECULAR BIOLOGY." *Integrative Biology: Quantitative Biosciences from Nano to Macro*. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3865110/

Wang, S. J., Brechbiel, M., & Wiener, E. C. (2003). "Characteristics of a New MRI Contrast Agent Prepared from Polypropyleneimine Dendrimers, Generation 2." *National Center for Biotechnology Information*. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/14501494

Watts, J. K., & Corey, D. R. (2011, Nov. 9). "Gene Silencing by SiRNAs and Antisense Oligonucleotides in the Laboratory and the Clinic." *The Journal of Pathology*. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3916955/

Weinblatt, M. E. (2013). "Methotrexate in Rheumatoid Arthritis: A Quarter Century of Development." *Transactions of the American Clinical and Climatological Association*. American Clinical and Climatological Association. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3715949/

Yu, B., Tai, H. C., Xue, W. Lee, L. J., & Lee, R. J. (2010, Oct.). "Receptor-targeted Nanocarriers for Therapeutic Delivery to Cancer." *Molecular Membrane Biology*. U.S. National Library of Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3789246/

Zhang, Y., Thomas, T. P., Desai, A., Zong, H., Leroueil, P. R., Majoros, I. J., & Baker J. R. Jr. (2010, Mar. 17). "Targeted Dendrimeric Anticancer Prodrug: A Methotrexate-Folic Acid-Poly(amidoamine) Conjugate and a Novel, Rapid, "One Pot" Synthetic Approach." *Bioconjugate Chemistry*. U.S. National Library of Medicine. Retrieved from http://pubs.acs.org/doi/abs/10.1021/bc9003958