Supplementary table 1. Analysis of examples for Forty Inventive Principles.

	Inventive Principle	**Number of occurrences in Contradiction table**	**Number of occurrences in my screening**	**Description**	**Definition of exemplar problem**	**Original abstraction of exemplar problem**	**New terminology of abstraction**	**Inventive solution of exemplar problem**
1	**Segmentation**	242	6	Divide object or system into scalable sections, make them easy to assemble, disassemble and modify. Optimize degree of segmentation.	Genome is too huge to be sequenced from start to finish.	4 – Length of stationary object *vs.* 36 – Complexity of device	Price *vs.* Turn-around time	Shotgun sequencing [6].
2	**Extraction**	222	4	Separate an interfering (weak) part or property from object/system, and/or identify crucial (sufficient) parts or	It is convenient to do PCR setup without cooling rack. However, Taq polymerase has unwanted	33 – Convenience of use *vs.* 30 – Harmful factors acting on subject	Specificity *vs.* Convenience	Separating pre-PCR polymerase activity by omitting magnesium [7].

				properties.	enzymatic activity at room temperature.			
3	**Local quality**	131	4	Exploit and/or increase heterogeneity of object, system or environment. Ensure each part functions in suitable conditions, and/or can fulfill a different useful and/or complementary function.	One round of PCR is sometimes insufficient to reach desired yield. Nested PCR can improve it but brings contamination-prone opening tubes.	26 – Amount of substance *vs.* 27 – Reliability	Sensitivity *vs.* Contamination	Closed tube nested PCR with second set of reagents in a hanging gel matrix[11].
4	**Asymmetry**	76	3	Introduce or increase asymmetry in the shape of object/system. Change shape or properties to suit	PCR produces large amount of double stranded amplicons. Some downstream	8 – Volume of stationary object *vs.* 31 – Harmful side effects	Specificity *vs.* Yield	Asymmetric PCR with concentration of forward and reverse primers differing in orders

				external asymmetries.	applications require to amplify just one DNA strand.			of magnitude [13] to produce excess of one DNA strand.
5	**Combination**	35	4	Bring together things that happen at the same time or place (merge, parallelize and/or consolidate). Make operations contiguous or parallel. Agglomerate objects or systems.	PCR can be adapted to amplify RNA template after its reverse transcription into cDNA. Opening tubes after reverse transcription generates possibility for contamination and biased amplification result.	35 - Adaptability *vs.* 28 - Accuracy of measurement	Yield *vs.* Robustness	Combined reverse transcription and PCR in closed tubes [16].

6	**Universality**	85	4	Make parts of object or system perform multiple functions, eliminate needs for other parts, use standardized features.	Different primers in PCR multiplex require different annealing temperatures to reach sufficient specificity and yield.	8 - Volume of stationary object *vs.* 17 – Temperature	Specificity *vs.* Yield	TouchDown PCR to level out hybridizing requirements of several primer pairs to ensure specificity with increased yield [23].
7	**Nesting dolls**	36	4	Place objects or systems sequentially inside others. Pass one part (dynamically) through a cavity in another.	One pair of primers is sometimes insufficient to identify similar alleles, related organisms, or background contamination.		Sensitivity *vs.* Convenience	Nested PCR [90].
8	**Counterweight**	44	2	To counteract the weight of	.During phenol chloroform DNA		Specifiicty vs. Yield *vs.*	Gel plugs in centrifuge tubes for

				object/system, combine it with others that provide lift or exploit buoyancy/other environmental forces.	extraction, upper, aqueous phase is transferred by pipetting to other tube for precipitation by ethanol. Sometimes interphase or lower phase is co-pipetted.		Convenience	separating aqueous and organic phases during DNA extraction (5PRIME Phase Lock Gel).
9	**Prior counteraction**	26	3	Anticipation of negative effects; apply measures to control harmful effects of actions with both adverse and useful effects; create stresses in object/system that	It is convenient to do PCR setup without cooling rack. However, Taq polymerase has unwanted enzymatic activity at room		Specificity *vs.* Convenience	HotStart Taq to reduce unspecific PCR priming [18].

				will oppose known undesirable stresses later.	temperature.			
10	**Prior action**	264	4	Anticipate requirements. Adjust object/system (fully or partially) before essential. Pre-arrange objects or systems to optimize convenience and minimize delay.	Mutant and wildtype alleles amplify with the same efficiency. However, the improved detection limit for a mutated allele in surplus of wildtype allele is often needed.		Specificity *vs.* Sensitivity	Blocking wildtype allele primers to increase PCR sensitivity to mutant alleles [19].
11	**Cushion in advance**	49	5	Anticipate failure. Prepare contingency measures to compensate for low reliability of	It is possible to decontaminate working surfaces and air after PCR. However, DNA-		Robustness *vs.* Specificity	Incorporating dU into PCR for postPCR decontamination by uracil N-

				object/system.	destroying substance can get into the subsequent PCR. More specific amplicon removal is needed.			glycosylase [22].
12	**Equipotentiality**	32	2	Redesign object's environment to raise or lower it, if necessary, or eliminate need to move it.	Different primers may require different annealing temperatures in PCR while it is advantageous to use them in one PCR run.		Specificity and Sensitivity *vs.* Convenience and Yield	TouchDown PCR starts with high annealing temperature that gradually decreases during next cycles. Thus, amplification by different primers is allowed while specificity of more sensitive primers is still retained [23].

13	**Inversion**	140	4	Invert action used to solve problem (e.g. heat instead of cool an object). Fix movable parts (or external environment), and make fixed parts movable. Turn the object (or process) 'upside down'.	PCR requires knowledge of two primer-complementary sequences to allow amplification. Sometimes sequence information for the second primer is lacking.		Preanalytical requirements *vs.* Specificity	Inversion PCR with 3´ends of primers facing outwards [24].
14	**Spheroidality or curvature**	83	4	Use curvilinear/spherical rather than rectilinear parts, surfaces or forms; rollers, balls, spirals or domes; shift from linear to rotary motion (or vice versa).	PCR tube caps and strips of caps are difficult to fully close by finger pressure.		Convenience *vs.* Price	Curved PCR tube capping aids (Eppendorf 951023108).

				Use centrifugal forces.				
15	**Dynamism**	159	4	Allow/design properties of object, environment, process or system to change in accordance with operating conditions. Divide object or system into parts that can move relative to each other, if it is rigid or inflexible make it movable or adaptive. Increase degree of free motion.	Failure during pipetting, air bubble, PCR inhibition, or other factor can cause false negative PCR.		Robustness *vs.* Convenience	Internal PCR standards in every tube allowing adjustment for uncontrollable factors [92].
16	**Partial or excessive action**	99	2	'Slightly' increase or decrease a procedure when perfect	We are interested in minority population with		Specificity *vs.* Yield	Reducing denaturation temperatures in

				optimization is impossible or too expensive.	mutation though majority is wildtype.			COLD-PCR to increase detection limit for minority DNA sequences [29].
17	**Moving to a new dimension**	87	3	If an object or system has or moves in a straight line or plane, consider use of dimensions or movements beyond the line/plane. Use multi-story rather than single-story arrangements, tilt or re-orient object/system, look at it from other angles, use other sides of given areas and/or other	Multiplexed real-time PCR technologies require complicated and costly design and manufacturing of separate detection probes for each new target.	39 - Productivity *vs.* 36 – Complexity	Sensitivity *vs.* Convenience	Use of unnatural nucleotide bases overcomes restrictions done by two “dimensions” of C-G and A-T nucleotide pairing and allow to design universal detection by energy transfer probes [30].

				scales.				
18	**Mechanical vibration**	161	7	Cause object or system to oscillate or vibrate, or increase frequency. Use resonant frequencies, piezoelectric rather than mechanical vibrators, or combined ultrasonic and electromagnetic field oscillations.	We want to postpone start of the second round in PCR within constraints of closed tube.		Specificity *vs.* Convenience	Vibrating PCR tubes to launch second round PCR in nested PCR [40].
19	**Periodic action**	158	4	Use periodic or pulsating rather than continuous actions, or change periodic magnitudes or frequencies. Use	DNA denaturation step before primer annealing uses high temperature that is harmful to polymerases.		Specificity, Sensitivity, Robustness, Price, Turn-around time, *vs.* Yield	PCR *per se* [42].

				pauses between impulses to perform a different action.				
20	**Continuity of action**	19	3	Make all parts of object/system work at full load, all the time. Eliminate all idle or intermittent actions or work.	PCR is based on cycling changes of temperatures. Heating and cooling using Peltier effect and or hot/cold air is rate limiting.		Convenience *vs.* Turn-around time	Pumping reaction mixtures through different temperature zones in PCR cycling [43].
21	**Skipping, rushing through**	37	2	Conduct destructive, harmful or hazardous process or operation rapidly.	High temperature is needed to conduct PCR; however, high temperature is deleterious to PCR reagents. It takes		Specificity *vs.* Turn-around time.	Fast PCR [45].

					ramp time to reach the correct temperature in thermocycler.			
22	**Blessing in disguise**	84	2	Exploit harmful (particularly environmental) factors to resolve a problem, or amplify them so much that they are no longer harmful.	Difference between strength of primer binding to its target and to false target differing in one nucleotide is not sufficiently discriminatory for PCR.		Specificity *vs.* Yield.	Mismatch increasing specificity of PCR [47]. While mismatch at 3´end of primer can make hindrance to amplification, deliberate mismatch at other primer position can increase difference in binding strengths between correct target template and

								incorrect template.
23	**Feedback**	35	3	Introduce or modify strength of feedback (referring back, cross-checking) to improve action, process or system.	Transparent PCR buffer in low volume is hard to distinguish during pipetting.		Specificity *vs.* Sensitivity, *vs.* Real Time monitoring	Cresol red as inert pipetting aid for PCR mixtures [49].
24	**Intermediary**	92	3	Use an intermediary carrier or process. Merge one object or system temporarily with another that can be easily removed.	Interface between upper phase with nucleic acids and interphase with proteins is easily disrupted and phases mixed by pipetting.		Specificity *vs.* Robustness	Use of gel plug during nucleic acid extraction with organic chemicals [51].
25	**Self-service**	49	3	Make object or system serve itself by performing auxiliary	One phosphate is released from nucleotide		Specificity *vs.* Real time	Inorganic phosphate release upon dNTP incorporation into

				functions (such as testing or maintenance). Use waste resources, energy, or substances.	triphosphate upon incorporation of nucleotide into the nascent nucleic acid strand by polymerase.		monitoring	nascent DNA strands for signal detection during pyrosequencing [53].
26	**Copying**	140	4	Use cheap, simpler copies rather than a scarce, fragile or expensive object or system. Replace object, system or process with an optical copy, and visible optical copies with infrared or ultraviolet copies. Look at things in another light.	Genomic DNA is consumed during testing.		Preanalytical requirements *vs.* Multi-targeting	Analysis of PCR amplified DNA rather than gDNA template [42].

27	**Cheap disposables**	121	4	Replace expensive objects/systems with cheap substitutes, provided they have acceptable qualities.	Nucleic acids are being obtained from organism in remote terrains without access to sophisticated instrumentation as well.		Robustness *vs.* Point-of-care sampling	Portable nucleic acid extraction system using bicycle pump [55].
28	**Replacement of mechanical systems**	229	2	Replace mechanical systems with sensory (e.g. optical or acoustic) systems or electric, magnetic and electromagnetic fields. Change from static to movable fields, and unstructured to structured fields. Use fields in conjunction	Even the best Peltier pumps in PCR blocks have temperature heterogeneities, affecting PCR analytical parameters.		Temperature homogeneity *vs.* Turn-around time	Heated air in PCR thermocycler instead of Peltier pump [58].

				with field-activated (e.g. ferromagnetic) particles. Use natural phenomena.				
29	**Pneumatics or hydraulics**	118	2	Use gas and liquid parts of object/system (e.g. inflatable, liquid- or air-filled, hydrostatic or hydro-reactive parts) instead of solid parts.	Miniaturized valves only modulate the flow of the dispersed phase. On-demand generation of droplets with precisely defined size, frequency, and timing is needed.		Real time parameter adjustment *vs.* Timing	Integrated pneumatic micropumps for droplet generation in lab-on-chip [59].
30	**Flexible films or membranes**	63	5	Use flexible shells and thin films instead of three-dimensional	While PCR plates enable simultaneous		Specified tube format *vs.* Automation	Membrane array rolls for SNP genotyping [61].

				structures to separate, isolate, and protect sensitive samples/components in order to improve costs, space requirements and flexibility.	testing of (96, 192, 384, or 1536) templates in one run, the handling of plates requires robotic arm.			
31	**Porous materials**	47	4	Make object or system porous or add porous elements (inserts, coatings, etc.) for absorbing, filtering, and collecting liquids or gases that can be subsequently released in a controlled manner. Use pores, if already present, to introduce useful substance or	Cotton brushes were originally used for biological material collection for forensic DNA profiling. However, they were not satisfactory in terms of yield from minute DNA		Convenience *vs.* Yield	Porous brushes for trace DNA samples [63].

				function.	samples.			
32	**Changing colour**	146	4	Change colour or transparency of an object, system or its environment. To improve observability use coloured additives or luminescent elements, and/or change emissivity of objects subject to radiant heating.	Fluorophore attached to oligonucleotide probe should be switchable to mirror probing reaction.		Yield *vs.* Timing	Fluorescence resonance energy transfer (FRET) in oligonucleotide probes [64].
33	**Homogeneity**	31	3	Make objects or systems interacting with a given object of the same material (or material with identical properties).	Opening the tubes after downstream molecular genetics reaction brings risk of contamination. Therefore closed-		Convenience *vs.* Specificity	In AlphaScreen, singlet oxygen molecules travel from Donor beads to Acceptor beads within 200 nm

					tube or "homogenous" methods are needed.			distance and generate chemiluminiscent signal [93].
34	**Recycling, discarding, and regenerating**	105	4	Discard portions of object or system that have fulfilled their functions (e.g. by dissolution, evaporation, etc.) or modify them during operation. Conversely, restore consumable parts directly in operation.	Opening the tubes after downstream molecular genetics reaction brings risk of contamination. Therefore closed-tube or "homogenous" methods are needed.		Convenience *vs.* Timing	Wax layer barrier to sequester Phi29 pre-amplification from a target-specific real-time PCR reaction [68].
35	**Transforming physical or chemical**	411	2	Change physical state of object or system (e.g. to a gas, liquid, or	Though frozen DNA is quite stable, freezers		Price, Convenience, *vs.* Shelf life	Paraffin-, chitosan-, trehalose- or pullulan-

	properties			solid), concentration, consistency, flexibility, temperature, pressure, or other parameters.	consume energy, freeze-melt cycles are inconvenient and destroy DNA.			encapsulated archived DNA or PCR reagents [69].
36	**Phase transition**	60	4	Use controlled expansion, evaporation, cooling, or shape changes for catalytic effect during phase transition (i.e. via changes in volume and heat absorption).	DNA, separated by electrophoresis, is entrapped in agarose. Its easy release is needed.		Robustness *vs.* Convenience	Low melting temperature agarose for nucleic acid manipulation after electrophoresis [70].
37	**Thermal expansion**	60	2	Use thermal expansion or contraction of material (or multiple materials with different coefficients of thermal	During denaturation PCR step, pH increases and destroys DNA template. Also,		Robustness *vs.* Convenience	High pH PCR buffer to control pH reductions in high temperature PCR steps and reduce

				expansion).	PCR inhibitors in blood are active at low pH.			effects of contaminants in whole blood samples [72].
38	**Strong oxidants**	48	3	Replace air with oxygen-enriched air, pure oxygen, or ozone; expose air to ionizing radiation, replace standard air with oxygen-enriched air. Add an active ingredient.	Products from previous PCR can contaminate subsequent PCR even if present in low volume aerosol. Decontamination agent should diminish before next PCR setup.		Efficiency of decontamination *vs.* Timing	PCR decontamination by bleach [75].
39	**Inert environment**	77	4	Replace normal environment with an inert one, add neutral	Watson-Crick pairing of bases bears specificity		Specificity *vs.* Shelf life	Peptide backbone of peptide nucleic acid to hide sequence

				parts or inert additives to an object or system.	during nucleic acid hybridization. Sugar-phosphate backbone keeps nucleic acid together but is amenable to destruction by nucleases.			before nucleases [78].
40	**Composite materials**	94	4	Change from uniform to composite or multiple materials for synergistic effects.	Length separation of microsatellites by polyacrylamide electrophoresis of restricted length does not have sufficient resolution.		Separation *vs.* Length of moving object	Composite gel system consisting of anodal and cathodal zones, which differ by pore size and ionic strength to improve resolution of microsatellite alleles in polyacrylamide

								electrophoresis [80].